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INDICATIONS, TECHNIQUE AND RESULTS OF THE STEREOTACTIC OPERATIONS UPON THE HYPOPHYSIS USING RADIO-ISOTOPES[1]

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Since Spiegel and Wycis in 1947 introduced stereotactic operations in man, the field for this technique has enlarged. Stereotactic operations upon the hypophysis were stimulated by Luft and Olivecrona's (11, 12) demonstration of the value of hypophysectomy in the treatment of sex-linked carcinoma, of malignant diabetes and of other diseases. The stereotactic method offered a means of reducing the mortality of these operations and in addition a means of introducing radioactive isotopes into the hypophysis to produce an interstitial irradiation.

Wycis and collaborators (1954) reported upon a cystic craniopharyngioma, which was punctured using a stereotactic instrument, and a colloidal preparation of radioactive chromium and phosphorus introduced into the cavity. The general symptoms receded and vision was improved (31). In 1954 Talairach *et al.* (30) described a nasal route for stereotactic hypophysial operations. He published with Tourneaux in 1958 a very informative report of their experiences in 29 patients. In 52 per cent of cases, vision was improved and in 11 patients other symptoms receded. When it is considered that these authors operated on 12 patients in whom other techniques had failed, on some patients with extrasellar extension of the tumor and on some patients who were too poor risks for an open surgical attack, one must judge the results as favorable. Other authors who used a stereotactic apparatus for hypophysial operations include Forrest and Brown (4) and Ellis (3).

Our experiences with the stereotactic operations on the hypophysis were first reported in 1953; later the results in 62 patients followed for several years were described in 1956 (24). We constructed a "target" apparatus, with which we have performed (to December 10, 1959) a total of 848 stereotactic procedures for various conditions; 104 were directed at the pituitary. Our "target" apparatus has been described elsewhere (1951, 1956, 1959). It makes it possible to reach intracranial points from the cranial convexity as well as from the base of the skull with a precision of ± 0.5 mm. In the case of hypophysial operations, either transfrontal or transethmoidal (nasal) route is possible (Figures 1A, 1B).

TRANSFRONTAL APPROACH

The scalp and skull are punctured at the hairline, approximately 2 cm. lateral to the midline. A tape, the calibrations of which are radioopaque, is applied to the midsagittal plane of the head so that the most favorable angle of incidence with the pituitary fossa may be determined. The location of the small scalp incision is scratched. By

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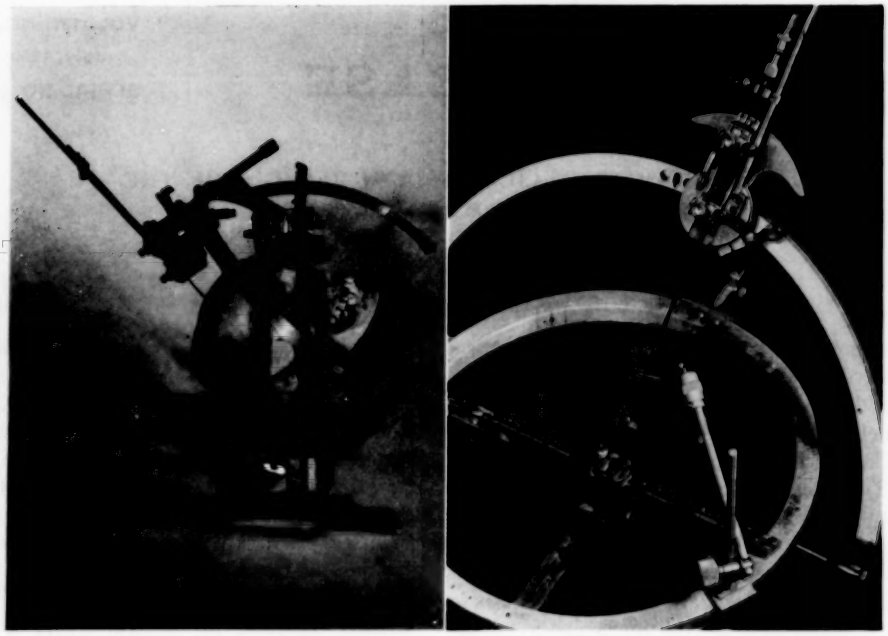

FIG. 1A FIG. 1B

FIG. 1A. Stereotaxic apparatus attached to the skull: The ring, fastened to the skull by means of six pins, is fitted to the U-shaped frame. The semicircular arm carrying the needle-holder—adjustable in any direction—rotates around the interauricular line of the ring. The angular positions of the exploring needle are measured mechanically on the phantom-ring.

FIG. 1B. The phantom-ring, used for determination of angular positions, is identical with the ring applied to the head (Figure 1A). On the phantom-ring a system of coordinates, related to the three dimensions of space, allows the target-point, calculated from the three planes in roentgenograms of the skull to be represented within the phantom and its position referred to the coordinates. The needle, carried by the needle-holder on the arm, is directed through the phantom trephine opening and brought into contact with the phantom target (on top of the vertical coordinate). The coordinates are then read off from the phantom ring.

using a small trephine directed toward the pituitary fossa, one may make a hole large enough for the exploring needle and yet so small that the scar is not dimpled to mar the cosmetic effect. The needle is introduced into the sella between the two anterior clinoid processes. In case of a prefixed chiasm, which is present in five per cent of people, the optic nerve may be subject to injury, unless the needle is carefully inserted. The length of the anterior clinoid processes can be estimated on slightly oblique roentgenograms of the skull.

Our technique is to apply the ring after infiltrating the sites of the cranial pins with a local anesthetic agent. The needle is introduced in the planes calculated on the phantom ring and under control of the image intensifier to the level of the optic nerve (Figure 2). Here cisternal fluid frequently escapes, and a few cubic centimeters (3–4 ml.) of air may be injected to visualize the basal cisterns. On roentgenograms of the skull the distance between needle point and intrasellar target point is measured and corrected for distortion. The needle is slowly advanced to this point while the visual acuity and fields are being checked. On piercing the diaphragma sellae, the operating surgeon encounters a slight re-

sistance and the patient feels a stinging pain behind the eyes.

Once the needle is in place, a cyst may be aspirated, the gland electrocoagulated or a radioactive isotope may be implanted within the hypophysis. Beads of an ionizing substance may be distributed in geometrical patterns by a special needle (Mundinger, 1959) to obtain uniform destruction of the gland. Selected areas of the hypophysis can be coagulated with a movable "electrosound."

FIG. 2. Transfrontal approach for destruction of the hypophysis by a suspension of radioactive gold-graphite. The cannula is inserted into the sella between the anterior clinoid processes just in front of the optic chiasm.

TRANSETHMOID APPROACH

If the sella is to be approached through the ethmoid air cells or through the sphenoid sinus, the stereotactic bow is swung below the ring and the needle is inserted through a small skin incision. The single lamellas of bone are perforated with a sharp mandrin. This approach is preferred for hypophysectomy if the pituitary fossa appears radiologically normal or in the case of very large adenomas extending into the sphenoid sinus if an open transcranial operation is inadvisable (Figure 3). After this procedure the postirradiation edema induces fewer deleterious effects than that following a transfrontal puncture.

Radioactive isotopes employed: Interstitial ionization with isotopes offers the following advantages over other methods of tissue destruction:

1. The location of the maximal radiation effect is within the tumor or the tissue that is to be destroyed by radio-necrosis.

2. The extent of the radio-necrosis can be predicted by a knowledge of the dosage, distribution and the physical qualities (type, energy and half-life) of the isotope. The duration of the destructive process may be controlled within limits by consideration of half-life activity of isotope.

3. By choosing the isotope of a desired half-life and potency and using it in a liquid or solid form, one may be able to infiltrate the tissues or confine the isotope to the area of the target-point, thus preventing unde-

FIG. 3. Transethmoidal instillation of suspension of radioactive gold-graphite. The cannula enters the enlarged and distorted sella through the ethmoid and sphenoid sinuses (in a case of chromophobe adenoma).

sirable dissemination of the radioactive material through the cerebrospinal fluid or through the blood.

These are the main reasons for the use of radioactive isotopes. In contrast to the interstitial irradiation of voluminous hemispheral tumors which we believe should be treated with gamma emitters (Mundinger and Riechert, 1956, 1959), for pituitary tumors as well as hypophysectomy we prefer pure beta emitters, or isotopes with mixed rays, the gamma component being so low in comparison to the beta radiation that its effect may be neglected. In such cases irradiation damage to neighboring structures, optic chiasm and nerves as well as the hypothalamus must be avoided as far as possible.

We have used the following radio-isotopes:

1. *Phosphorus* (P^{32}, half-life of 14.3 days), as a molybdenum compound. It is put in tiny methacrylate capsules, made radioopaque by silver sheets. For hypophysectomy we insert usually three or more capsules, depending upon the size of the desired lesion. A capsule of P^{32} (1.69 MEV beta radiation) usually produces approximately a 3 mm. spherical lesion. The capsules are arranged in such a geometrical form as to cause maximal destruction in the sella. The average activity of each capsule is 1 millicurie.

2. *Gold* (Au^{198}, half-life of 2.7 days), mainly used since 1955. Seeds of radioactive gold have been inserted in three cases in open transethmoidal operations. As numerous histological examinations have proved, it is not the beta but the 0.4 MEV-gamma radiation of the gold which is the effective necrobiotic agent. The beta radiation produces only a necrotic margin 1–2 mm. in thickness around the seed. The dense gold (19.33) absorbs much of the 0.9 MEV beta radiation which penetrates only 0.1 mm. about the seeds, thus affecting only a thin shell of surrounding tissue.

In order to employ efficiently the beta radiation of radioactive gold, we have used a macromolecular suspension of gold adsorbed on graphite in a 40 per cent solution of glucose; this is prepared with an electric shaker shortly before use. For protection from radiation, it is then drawn up in a lead syringe with slitted windows and 0.1–0.2 ml. is injected in each of three or four sites in the pituitary fossa. Thus, as experiments have shown, the radioactive gold graphite is well distributed within the sella turcica so that the beta rays are effective throughout a greater volume than is possible when seeds are used.

The radioactive gold injected in this way remains in the pituitary fossa for numerous studies of spinal fluid, blood and the larger organs have failed to disclose ionization. Hence none of the radiation is lost from the sella turcica, as may occur if injections of colloidal gold are made, according to the observations of Rothenberg *et al.* (28) and Davies (1).

The activity of the injected material is measured with a collimating radiation detector and intensifier (Figure 4). The desired amount of activity depends on the size of the sella turcica, ordinarily being 10 to 25 mC, but in case of a very large pituitary tumor being as great as 35 mC. The absorption dose, assuming a homogeneous distribution, always amounts to more than 150,000 rep/ml of tissue. A certain variation in the distribution of beta activity, especially in the marginal areas, is effectively balanced by the gamma rays.

Yttrium (Y^{90}, half-life of 2.6 days), a pure beta emitter with 2.2 MEV, is used as yttrium oxide in a suspension. However, our experiences are too few to enable us to estimate to what an extent Y^{90} might have advantages over the radioactive gold-graphite suspension described above. Other authors (2, 10, 13, 19, 29) have reported good results with radioactive yttrium, in the form of rods of yttrium oxide, for hypophysectomy. Since the introduction of radioactive isotopes, electrocoagulation or puncturing of the hypophysial fossa has been carried out only in a few cases in which a selective

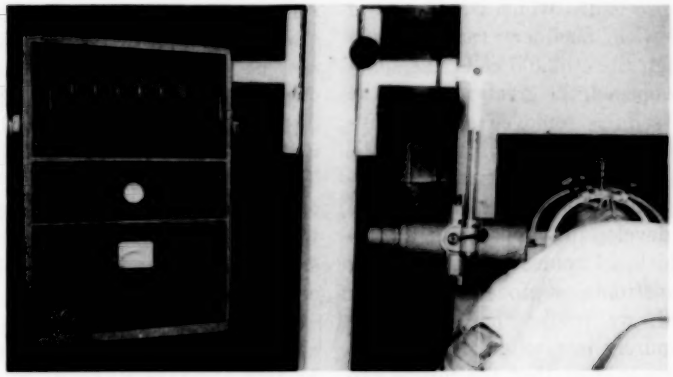

FIG. 4. Arrangement for recording of activity of radioactive gold-graphite instillate. The detector collimater is directed to the hypophysial fossa.

TABLE 1

Procedures and Conditions Treated in the Series of 83 Patients

Procedure	Number of procedures performed for									Total
	Chromophobe adenoma	eosinophile adenoma	basophile adenoma	craniopharyngioma	malignant hypertension	sex-linked cancer	diabetes mellitus	glioma	chordoma	
P^{32} molybdenum	5	7	1	1		3				17
P^{32} chromic				1						1
Au^{198} graphite (suspension)	30	13		2		5	1	1	1	53
Combination of P^{32} molybdenum and high frequency coagulation	4	3		1						8
Combination of Au^{198} seeds and high frequency coagulation						1				1
High frequency coagulation	7	2	3		5	1				18
Total	46	25	4	5	5	10	1	1	1	98
%	46.9	25.6	4.1	5.1	5.1	10.2	1.0	1.0	1.0	100%

destruction is desired, for example of the posterior lobe.

CONDITIONS WHICH MAY BE TREATED BY STEREOTACTIC PROCEDURES ON THE HYPOPHYSIS

Table 1 reports the conditions which we have treated by stereotactic operations upon the pituitary gland.

From the surgical point of view, it is advisable to discuss operations upon 1) the normal and 2) the enlarged pituitary fossa.

Operations upon the normal sella turcica: Hypophysectomy for sex-linked carcinomas, malignant diabetes, malignant hypertension, and Cushing's disease is carried out on a normal sized pituitary fossa. Even in such cases, the danger of damaging adjacent structures is very slight owing to the precision of our method (±0.5 mm.). Once, in a case of malignant hypertension we had a paresis of the nervus abducens due to a faulty adjustment of the needle. This paresis, however, receded within a few weeks.

If the patient's poor condition precludes a major procedure, the transethmoidal approach to the pituitary fossa is preferred. We have achieved a radical destruction of the hypophysis with a combined surgical-

stereotactic procedure, which we devised in cooperation with Zoellner. Inserting the needle through the ethmoid cells, the sphenoid sinus is opened, the greater part of the base of the sella is removed and the hypophysis is curetted out as fully as possible. Then radioactive isotopes are inserted. Following this procedure, we have had a spinal fluid fistula develop in two patients, a complication which, of course, does not occur when the transfrontal approach is used.

In general, we prefer the stereotactic method for purely intrasellar lesions, since it has become evident that the needle can be introduced without difficulty even if the fossa is not enlarged. This procedure is a simple one which can be performed on patients who are poor surgical risks.

Operations on the enlarged sella turcica: Dilatation of the pituitary fossa is usually due to a tumor which often extends through the diaphragma sellae. In such cases, the nature and extent of the tumor must be ascertained, if possible by an open operation after pneumoencephalography or angiography, for the extent and nature of the tumor is a prerequisite for a stereotactic procedure. An open procedure is especially advisable in those cases in which the tumor, after breaking through the diaphragm sellae, extends into the middle cranial fossa. Even though, by a transfrontal or transethmoidal approach, the insertion of radioisotopes would be easy because of the enlarged sella and the stretching of the chiasm and the optic nerves, visual difficulties are apt to occur as tension develops on the capsule due to the swelling of the tumor during the period of neurobiotic reaction, which will begin within three to four days. Clinically this will become apparent as deterioration of visual function. We have had to perform open operations in three cases in the first days after the stereotactic implantation of capsules of radioactive phosphorus. We observed that the puncture wound had healed, but that there was extreme tension on the capsule. For this reason we are reluctant to use stereotactic operations for large tumors, which have caused a considerable loss of vision. Only, if the disease is advancing and the general state of the patient does not allow an operation, will we consider a stereotactic procedure. Tourneaux is much more inclined to operate upon tumors with a suprasellar extension. He treats by stereotactic procedures adenomas with suprasellar extension and—mainly because of the low risk—every new growth that extends backward and towards the third ventricle. It may be that the transethmoid approach, which he mainly uses, is responsible for the good results.

POSTOPERATIVE IRRADIATION OF HYPOPHYSIAL TUMORS BY STEREOTACTIC METHOD

Irradiation with ionizing substances following an open operation for a pituitary tumor may be carried out by stereotactic procedures. When a tumor cannot be removed completely, or when a recurrence has developed, irradiation is advisable. In case of a hypophysectomy, if the clinical findings suggest that a complete removal was not accomplished, further destruction may be accomplished by stereotactic implantation of an ionizing substance.

These are the advantages of such irradiation:

1. A secondary craniotomy for recurrence of symptoms from a pituitary tumor is difficult due to scarring. This sequel does not hamper a stereotactic operation, which can be repeated without cicatrizations threatening the prognosis. At the present time, in anticipation of a secondary procedure we carry out certain procedures at the open operation after removal of the tumor to prepare for and to facilitate subsequent irradiation by a stereotactic method.

The point between the two anterior clinoid processes, where the needle is to be introduced into the sella turcica, is marked by a small steel pin inserted in the bone by a special instrument. With a graduated

dissector bent to fit the anatomical contours, the distance from this pin to the anterior margin of the optic chiasm and to the two optic nerves is measured and recorded. Thus the desired point for insertion of the needle into the diaphragma sellae can be ascertained by radiography and used as a target for subsequent stereotactic operations without fear of complications due to injury of the optic nerves or chiasm.

In addition, at the primary stereotactic operation, a small cannula can be inserted in the frontal perforation and fixed in the proper direction to be used as a guide for the introduction of the needle at subsequent procedures. Thus further stereotactic insertions of a needle may be performed with only routine radiological controls. In our experience the danger of acute tension on the capsule due to post-irradiation swelling has been minimal after an open operation, since the split capsule allows its contents to extrude.

2. Stereotactic postoperative irradiation of a pituitary tumor is possible, even if the general condition of the patient makes it inadvisable to do more than expose and incise the capsule of the neoplasm. Knowing the type of tumor and having coagulated a portion of the capsule, one can puncture the sella turcica after the wound has healed without stress on the patient. The late results are so favorable that we anticipate a wide field for use of the technique. The results of stereotactic operations are apparent from the data on mortality rate (Table 2), and on the recession of symptoms and signs related to the visual and endocrine systems (Tables 3, 4). In assessing these results it should be taken into consideration that stereotactic operations are carried out on patients who could not be operated upon otherwise because of their general state of health, their age or local cerebral conditions.

These findings show, that stereotactic operations on the hypophysis do not replace the open procedures, but under certain circumstances they give results which otherwise could not be obtained. For this reason they represent progress in hypophysial surgery.

TABLE 2

Age Distribution and Mortality Rates of 83 Patients Having Stereotactic Operations

Age range	N
10–19	8
20–29	12
30–39	16
40–49	22
50–59	21
60–69	4
Deaths within 1 year of operation*	13
Deaths in 2nd year after operation	1
Deaths in 3rd and 4th year after operation	3
Deaths from 4th to 7th year after operation	1
Total	18 (22%)
Survival rate (follow-up period of 7 years)	65 (78%)

* The relatively high mortality rate of the first year is due to the death of patients having hypophysectomy for cancer or having large suprasellar inoperable tumors.

SUMMARY

Based on our experience gained from 104 stereotactic procedures upon the hypophysis, technique and indications are presented. The operations were performed with our own stereotactic apparatus, which is also used for other intracerebral procedures such as pallidotomy, thalamotomy, fornicotomy, etc. Operations on the normal hypophysis (hypophysectomy) or on hypophysial tumors were performed through the transfrontal or the transnasal approach, using varying dosages and forms of radioisotopes for necrobiosis. Postoperative irradiation using stereotactic procedures are dealt with in some detail and the results tabulated. The stereotactic method of operation combines the advantage of low mortality and high tolerance in aged patients or patients who are poor surgical risks.

TABLE 3

Visual Status Following Stereotactic Operations: Evaluation of 35 Primary and 48 Secondary Stereotactic Operations with a Follow-up of 7 Years (1953–60)

State of individual eyes	Visual Acuity				Visual Field			
	Primary		Secondary		Primary		Secondary	
	No.	%	No.	%	No.	%	No.	%
Unaltered normal	50	65.8	52	53.1	44	56.6	36	35.3
Moderate improvement	1	1.3	11	11.2				
Fair improvement			5	5.1	5	6.4	22	21.6
Very good improvement	3	3.9	1	1.0				
Unimproved	10	13.2	17	17.3	12	15.4	33	32.4
Moderate impairment	1	1.3	8	8.2				
Transient impairment	3	3.9	1	1.0			2	1.96
Impairment	4	5.3	3	3.1	17	21.8	8	7.8
Marked impairment	4	5.3					1	0.98
Number of eyes	76	100%	98	100%	78	100%	102	100%

TABLE 4

State of Endocrine Function in 23 Hypophysial Adenomas

	Pre-operative No. cases	Post-operative No. cases
Number of patients with clinical evidence of moderate insufficiency of:		
Hypophysis	7	9
Adrenal cortex	5	5
Number of patients requiring administration of:		
Testosterone	2	6
Cortisone	1	2
Estrogen		1
Decortin		2
Multiple hormones		5

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NEUROPATHY WITH MALIGNANT TUMOR METASTASES

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Since the report of Denny-Brown in 1948 (6), there has been considerable and sustained interest in cases of polyneuropathy accompanying malignant tumors. This report was concerned with two patients who had predominantly sensory symptoms and signs. In each patient the tumor, unsuspected during life, was a bronchogenic carcinoma. Subsequent publications have recorded examples of carcinoma of the lung with polyneuropathy of sensory, motor and sensorimotor character (2, 9, 11, 12, 14, 16), and an association of neuropathy with carcinoma of organs other than lung has also been observed (2, 7)[3]. More recently the association of sensorimotor polyneuropathy with multiple myeloma (17) and of "peripheral neuropathy" with malignant lymphoma (13, 18) has excited comment.

In most accounts, whatever the nature of the concurrent malignant neoplasm, the history and course of the illness have excluded dietary deficiency as a cause of the peripheral nerve lesions. It is also noteworthy that, when nervous tissue has been available for anatomical examination, no evidence of tumor metastases to the peripheral nerves has been found. Both of these facts have suggested a "metabolic" or "toxic" basis for the neuropathy, and the production by the tumor of an antimetabolite which interferes with pantothenic acid or vitamin E metabolism has been postulated (6). To date, however, no evidence to support these postulations has been forthcoming and the nature of the presumed defect in the metabolism of peripheral nerves remains unknown.

The central purpose of the present communication is to present a group of cases of polyneuropathy accompanying malignant lymphoma and multiple myeloma (and one case of di Guglielmo's disease) in which the peripheral nerves were involved by multiple, focal, metastatic deposits. Intimately associated with tumor infiltrates were foci of demyelination with relative preservation of axis cylinders. A more diffuse demyelination accompanied the focal lesions and was attributed to Wallerian degeneration of focally damaged nerve fibers. In the majority of this group of cases clinical signs of symmetric sensorimotor polyneuropathy were evident during life. It is contended that the clinical and anatomic findings are explained by the presence of multiple tumor metastases which led directly to compression and demyelination of nerve fibers.

A second group of patients will be described briefly to illustrate the severe demyelination which may attend localized cancerous infiltrations of cranial and spinal nerves and nerve plexuses. None of the patients of this second group presented a picture of symmetric polyneuropathy at any time. Rather, they suffered from the banal cranial and radicular palsies commonly observed in carcinoma. Nonetheless, the anatomical picture of compression-demyelination which attended these local metastases

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to nerves exemplifies a process basically similar to that accompanying the widely disseminated lesions of the first group, and its illustration would appear pertinent.

CASE REPORTS: GROUP 1

MULTIPLE MYELOMA

Case 1:[4] A 59 year old woman was admitted to Montefiore Hospital on May 29th, 1935. From May, 1933, she had had intermittent pain of the right upper arm. In June, 1934, she complained of tingling in all the finger-tips. In ensuing months there were two episodes of unexplained fever. On January 1st, 1935, "peculiar" uncomfortable sensations involved both hands and all fingers and were accompanied by a sense of warmth. She was admitted to another institution on January 15th. There, she manifested persistent low-grade fever and persistent anemia (hemoglobin 48 to 62 per cent). Her urine contained a trace of albumin. Neurologic examination disclosed diminution of pain, touch and temperature sensation "distally over the hands and legs." Vibration sense was "diminished in the lower limbs." Slight atrophy and weakness of the intrinsic hand musculature was noted bilaterally. From January 15th to the time of transfer to this institution on May 29th, objective and subjective sensory disturbance remitted completely, but the atrophy of the hand muscles increased and wasting of the musculature of the forearms and lower limbs appeared.

On admission to this hospital the patient was noted to be pallid and obese. There was a soft systolic mitral murmur. Neurologic examination confirmed the atrophy and weakness described above. The knee jerks were depressed, but the other tendon reflexes were active. Any superficial sensory loss was questionable. Vibration and position sense were impaired in the toes. There were no fasciculations. The neurologic diagnosis was and remained "polyneuritis of unknown cause."

Pertinent laboratory results were as follows: 1 to 3 plus albuminuria; urine positive for Bence-Jones protein on August 2nd; hemoglobin 45 per cent; gastric analysis normal; spinal fluid protein 31.3 mgm. per cent; serum proteins normal. Roentgenographic survey of the skeleton disclosed a mottled appearance of the lower end of the right humerus.

In July, 1935, the patient showed generalized weakness which progressed. Paraesthesiae returned in all limbs. She complained of severe pain in the right elbow and on August 2nd sustained a fracture of the right humerus following a trivial trauma. Death occurred on August 4th, 1935.

Examination of the general organs disclosed the following: plasma cell myeloma of the right humerus with recent fracture; generalized amyloid disease (marked); hyperplasia of bone marrow; extramedullary hematopoiesis in the liver and spleen.

The spinal cord and peripheral nerves were normal macroscopically. Both brachial plexuses and both sciatic nerves were removed. Microscopically, Spielmeyer stains showed moderate diffuse demyelination of the aforementioned nerves. In Bielschowsky preparations axis cylinders showed only slight diffuse abnormality. There were numerous perineurial and endoneurial infiltrates of myeloma cells (Figure 1). Associated with these aggregates of tumor cells were foci of severe demyelination and axis cylinder degeneration, though the latter change was less severe. The posterior columns of the spinal cord showed ascending demyelination. There were no myeloma infiltrates in the spinal roots or spinal leptomeninges in many cord sections. Amyloid

[4] This case has been reported previously (5) and has been widely quoted in the literature. Our interpretation of the peripheral nerve lesions is based on a re-examination of the old material (which consisted of Spielmeyer and Bielschowsky preparations only) and the use of newly prepared hematoxylin-eosin stains.

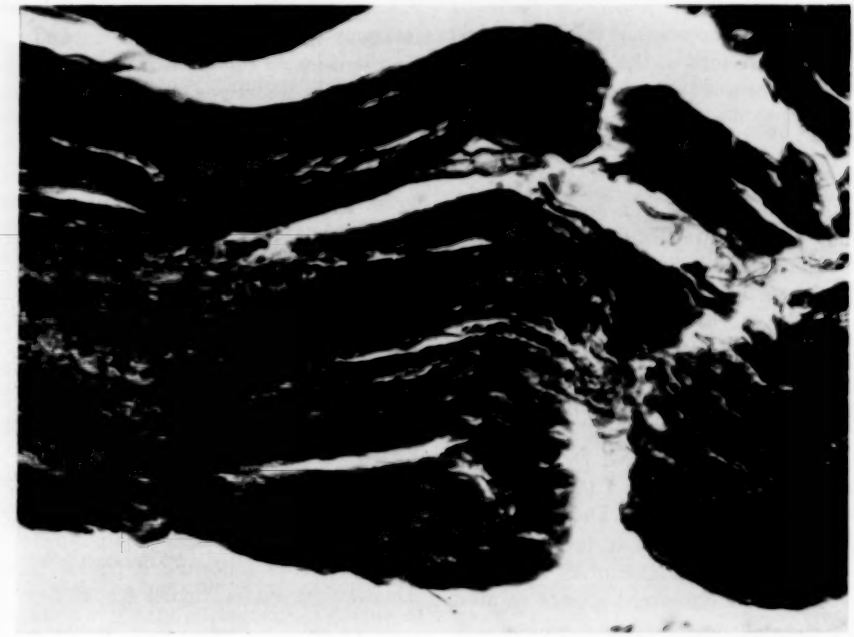

FIG. 1. Case 1. Myeloma cellular infiltrate in left brachial plexus. Hematoxylin-eosin stain. ×260.

infiltration of neural connective tissue was not present.

Case 2: A 67 year old male was admitted to Montefiore Hospital on November 22nd, 1957. In October of that year personality change and bizarre behavior were observed. At another hospital paresis of the wrists and hands and hypalgesia and hypesthesia of both lower limbs were noted. A diagnosis of peripheral neuropathy was made. There was no response to parenteral vitamin therapy. Admission examination on transfer to this institution elicited the following pertinent abnormalities: hepatosplenomegaly; a temperature of 102°F.; restlessness and confusion; bilateral grasp reflexes. There was no obvious paresis of the limbs and the deep tendon reflexes were normal. Adequate sensory testing was not possible because of the patient's restlessness and confusion. Indeed, neurological examination was generally unsatisfactory.

The patient had a past history of diabetes mellitus controlled by dietary restriction.

Pertinent laboratory findings were as follows: hematocrit 27 per cent with a hemoglobin of 9.0 gm.; fasting blood sugar 318 mgm. per cent; normal spinal fluid manometrics, protein and cell count; a bone marrow aspirate suggestive of multiple myeloma; an electrophoretic pattern of serum proteins suggestive of myeloma.

The patient remained confused and febrile. He became azotemic, developed fluid and electrolyte abnormalities, and died on December 6th, 1957.

The following anatomical diagnoses were made from examination of the general organs: plasma cell myeloma involving bone marrow, spleen, lungs and kidneys; pulmonary congestion and edema; nephrolithiasis and mild chronic pyelonephritis; cholelithiasis.

Save for atrophy of the frontal gyri, the

brain and spinal cord were normal grossly. The median and popliteal nerves and the brachial plexuses had a normal macroscopic appearance. Microscopic examination of the central nervous system disclosed invasion of the cerebrospinal leptomeninges by focal collections of plasma cells. These were present, too, in perivascular spaces in the cerebral cortex, centrum ovale and basal ganglia. Bielschowsky preparations revealed the presence of numerous senile plaques in both frontal cortices, and hematoxylin-eosin of numerous senile plaques in both frontal cortices. In hematoxylin-eosin sections of peripheral and spinal nerves there were numerous infiltrates of cells, identical morphologically with those which constituted the primary neoplasm. These cellular collections were both endoneurial and perineurial in location and were to be found in every section of nerve available (Figure 2). Spielmeyer and Bielschowsky stains showed mild or moderate alterations of myelin sheaths and axis cylinders throughout the length of each section, while in areas of tumor cell infiltration myelin sheaths and axons were destroyed or severely damaged (Figures 3, 4, 5). Sudanophilic material was practically limited to areas of neoplastic infiltration, where it was sometimes present within macrophages (Figure 6).

Case 3: A 60 year old woman was ad-

FIG. 2. Case 2. Myeloma cells among fasciculi of right median nerve. Hematoxylin-eosin stain. ×530.

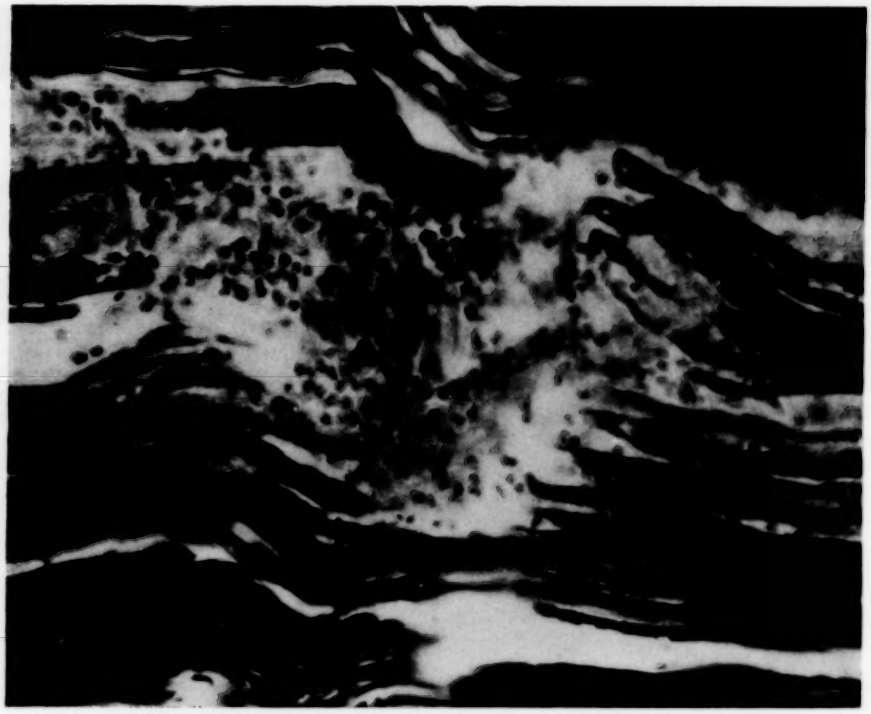

FIG. 3. Case 2. Myeloma infiltrate in left popliteal nerve with myelin sheath destruction. Spielmeyer stain. ×400.

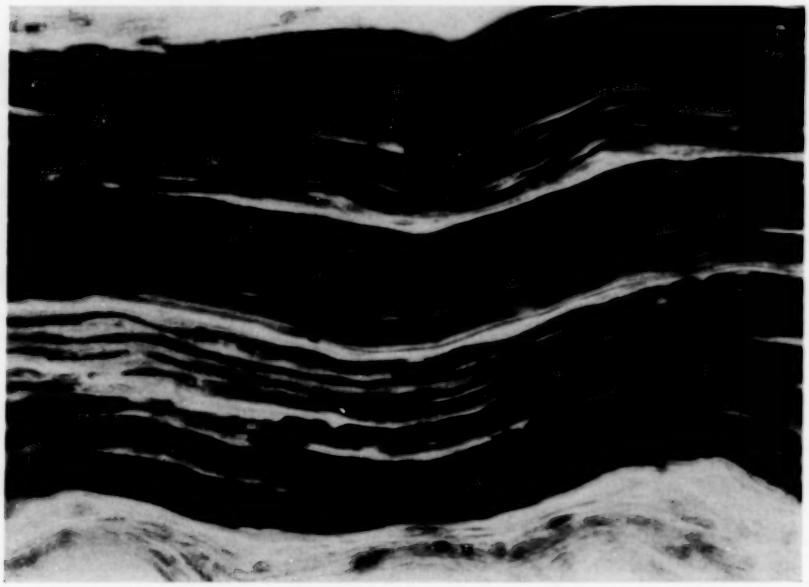

FIG. 4. Case 2. Diffuse fascicular demyelination in left popliteal nerve (same nerve as illustrated in Figure 3). Spielmeyer stain. ×400.

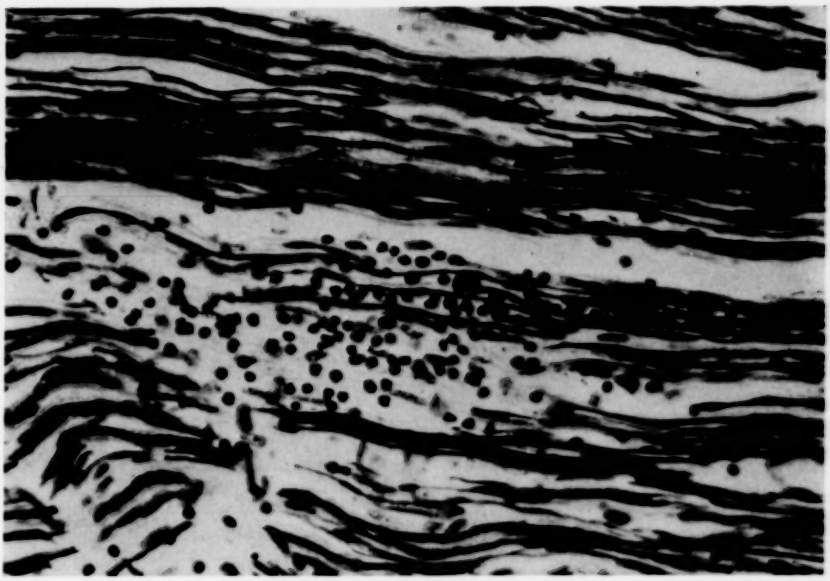

FIG. 5. Case 2. Fragmentation and swelling of axones in left popliteal nerve in vicinity of tumor infiltration. Bielschowsky stain. ×400.

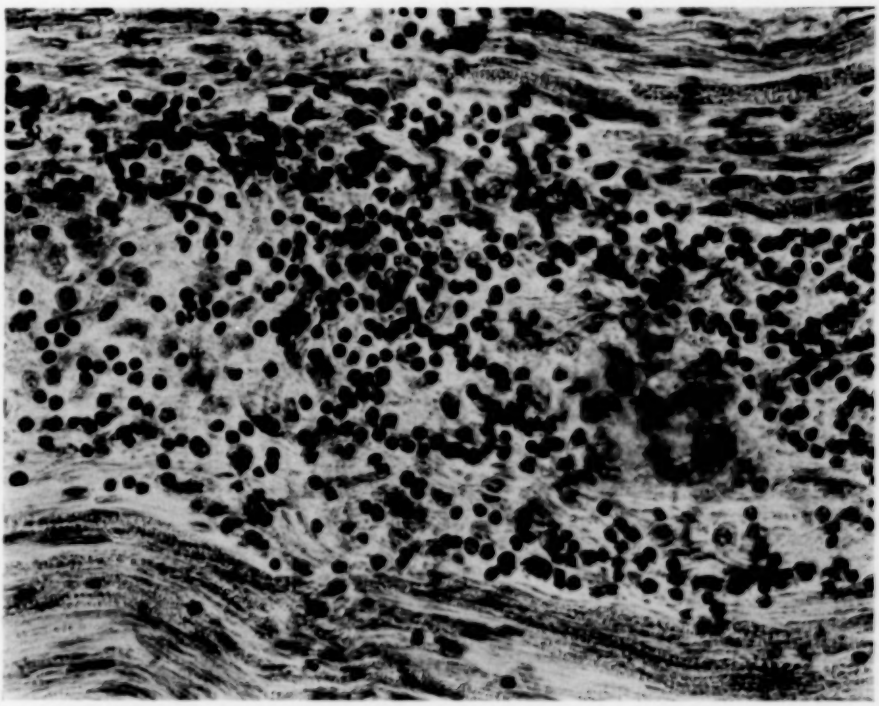

FIG. 6. Case 2. Clearly shown are many plasma (myeloma) cells and some sudanophilic material (fat) in large macrophages in left popliteal nerve. The fat appears as inconspicuous smudges in this black and white photomicrograph. Sudan III stain. ×400.

mitted to Montefiore Hospital on July 7th, 1955. In 1953 she had developed diffuse pain in the back. Subsequently she sustained a pathologic fracture of the femur. A diagnosis of multiple myeloma was made in January, 1955, on the basis of clinical and radiologic findings and examination of a bone marrow aspirate. Admission was necessitated by severe pain in the back which radiated into the right leg.

She was febrile and had an enlarged liver. Neurologic examination was normal except that vibratory sensation was diminished at the ankles and the right Achilles reflex was absent.

Pertinent laboratory data included a red blood cell count of 2.5 million per cu. mm. with marked rouleaux formation and a spinal fluid protein of 460 mgm. per cent. Spinal fluid manometries were not recorded. The entire skeleton was markedly osteoporotic to roentgenographic examination and there was a large defect in the first and second sacral vertebrae.

Shortly following admission the patient complained of numbness of both legs and "cutaneous sensation" was noted to be "impaired." Unfortunately, a detailed neurological evaluation was not done. Paraparesis and urinary incontinence first appeared on July 21st. She became jaundiced, uremic, comatose and expired on July 31st.

Autopsy disclosed multiple myeloma with widespread involvement of bone and spread to the liver, lymph nodes, pancreas, kidneys, adrenals, heart, ovaries and stomach. There was severe nephrocalcinosis.

The 11th dorsal vertebra was collapsed and there was a mass of epidural neoplasm at this level. The underlying segments of the spinal cord were compressed. The femoral nerves and the psoas muscles were removed. They had a normal macroscopic appearance. Hematoxylin-eosin preparations of the psoas muscles revealed massive infiltration by streams of myeloma cells. Intervening muscle fibers were compressed and their sarcoplasm was homogeneous and deeply eosinophilic. Microscopic preparations of the femoral nerves showed infiltration of the epineurium and perineurium by tumor cells which formed a dense sleeve-like investment. In Spielmeyer and Kultschitsky stains, the femoral nerves exhibited severe demyelination.

MALIGNANT LYMPHOMA AND BLOOD DYSCRASIAS

Case 4: In April, 1953, at age 54, this white male noted a burning sensation in the tips of the fingers which was exaggerated by warmth. Weight loss and anorexia appeared in January, 1954, and he was found to have a mass in the left hypochrondrium. On admission to another institution a red blood cell count of 10.8 million and a white blood cell count of 76,000 (mature neutrophiles 53 per cent; immature neutrophiles 33 per cent; myelocytes 7 per cent; lymphocytes 5 per cent; monocytes 2 per cent) were discovered. A bone marrow aspirate was reported as consistent with a diagnosis of erythremia. Splenectomy was performed and the patient was discharged. His appetite improved and he regained weight. However, in August, 1954, paraparesis and urinary incontinence appeared and he was admitted to Montefiore Hospital the following month after an episode of severe epistaxis. A hemogram on September 20th, 1954, disclosed a hemoglobin of 8.5 gm.; red blood cell count of 2,900,000; white blood cell count of 111,200 with 73 per cent neutrophiles, 4 per cent stab forms, 6 per cent metamyelocytes, 9 per cent basophiles, one per cent monocytes and 2 per cent abnormal forms; and a platelet count of 128,700. A diagnosis of chronic myelogenous leukemia was entertained and a bone marrow aspirate was read as consistent with this diagnosis.

Neurological examination on October 6th, 1954, disclosed a somewhat cachectic man with double incontinence and sacral decubiti. There was notable wasting of the legs and of the small muscles of the hands bilaterally. The tendon reflexes were hyper-

active throughout but symmetrical and there were equivocal plantar responses. There was weakness of the distal limb musculature. Sensory alterations included bilateral "glove and stocking" hypalgesia and hypesthesia and bilateral impairment of position sense in the toes. He complained of painful paresthesiae of all limbs. A cystometrogram revealed an atonic bladder. Electromyography disclosed "fibrillation potentials" in the right flexor carpi radialis and right biceps as well as "very narrow biphasic potentials" on contraction.

A diagnosis of polyneuropathy and myelopathy was entertained. The cause was not suggested. Large oral doses of a multivitamin preparation as well as parenteral administration of 500 mgm. of pyridoxine, 100 mcg. of vitamin B12 and 10 mgm. of thiamine were instituted on a daily basis. A course of total body irradiation was given. Urinary infection was controlled by antibiotics. On November 20th, 1954, he had received vitamins as described for more than five weeks and had completed 200 r of total body irradiation. The neurologic status and hematologic picture were unimproved. He complained bitterly of painful paresthesiae and the fingers and volar surfaces of the hands were painful to touch. Myeleran, in a dosage of 6 mgm. daily, was started on November 29th, and on January 5th, 1955, the white blood cell count had fallen to 24,000 and the red blood cell count had risen to 5.3 million. The paresthesiae were greatly diminished and sphincter function returned to normal. Vitamins were discontinued. Myeleran was continued in a daily dose of 2–4 mgm. By April, 1955, the patient was able to walk unaided, had gained 30 lbs. in weight and was free of spontaneous pain. The leucocyte count varied between 40,000 and 60,000. In June, 1955, he remained well, but careful examination disclosed slight paresis of the lower limbs and hypesthesia and hypalgesia below the ankles. In ensuing months the blood picture reverted to one of polycythemia. However, the patient remained free of symptoms. Myeleran was discontinued in September. Neurologic examination on November 18th revealed no evidence of neuropathy, though the musculature of the lower limbs had a wasted appearance which contrasted with the normal appearing bulk of the upper extremities.

The patient's discharge was under consideration when, in January, 1956, a massive hematemesis occurred and radiologic examination showed a duodenal ulcer crater. He was treated by blood transfusion and a Sippy diet. On February 4th, 1956, he became jaundiced. The jaundice progressed rapidly and the patient went into shock and died on February 6th. No detailed neurologic examination was performed in the last three months of life.

Anatomic diagnoses on general autopsy were as follows: polycythemia vera and myeloid hyperplasia of bone marrow; erythroid infiltration of the myocardium, kidneys, liver, lymph nodes, parotid gland and cerebral dura; vegetative endocarditis of all cardiac valves; renal and cerebral embolic scars; duodenal and gastric peptic ulcers; chronic cystitis and pyelonephritis; focal necrotizing pneumonitis; focal hepatitis; jaundice.

The right median and left femoral nerves were removed at autopsy and appeared normal grossly. The body musculature had the normal red-brown appearance. The spinal cord and cauda equina were unremarkable save for chalky discoloration of the posterior columns at all levels.

Hematoxylin-eosin, Spielmeyer and Sudan preparations of the peripheral nerves were obtained and showed perineurial and interfascicular infiltrations of neoplastic cells composed of both myeloid and erythroid elements (Figure 7). Some of the tumor metastases were clearly perivascular in location. There was a mild to moderate diffuse demyelination with focal accentuation of myelin sheath alterations in areas of tumor infiltration. The nerve roots of the cauda

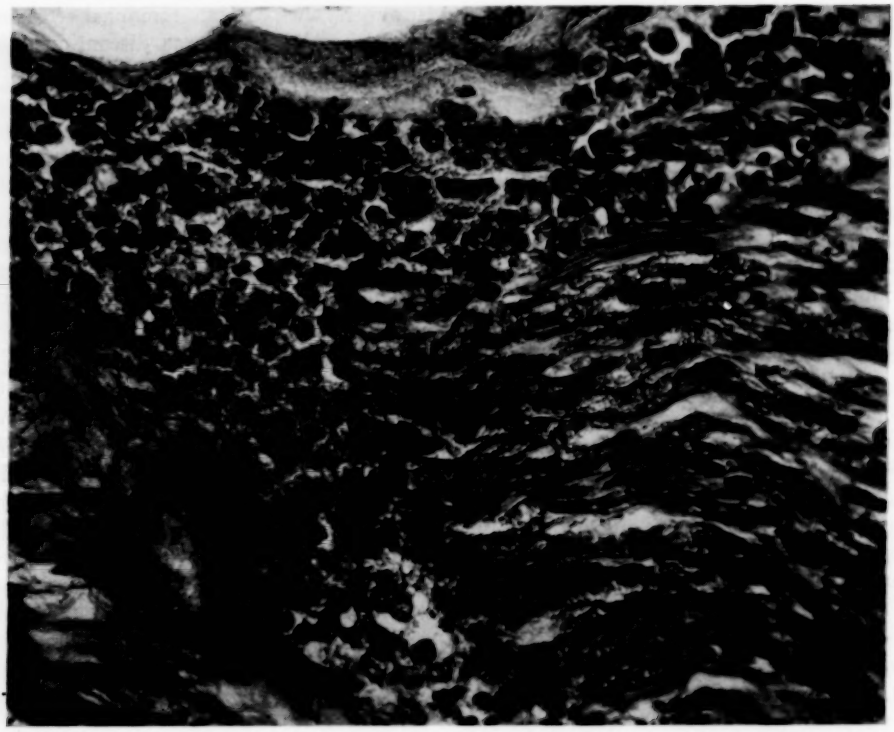

FIG. 7. Case 4. Interfascicular infiltration of immature, nucleated red cells in peripheral nerve. Note foamy degenerating myelin sheaths. Hematoxylin-eosin stain. ×400.

equina showed a similar picture. The posterior columns of the spinal cord were demyelinated at all levels. A single lumbar posterior root ganglion was examined and was normal histologically. Only a single section of gastrocnemius muscle was available. It showed an interesting process: there was massive infiltration of the muscle by neoplastic myeloid and erythroid elements with extensive replacement and degeneration of muscle fibers. At first glance the microscopic appearance suggested a suppurative myositis. There were no neoplastic infiltrations of the spinal leptomeninges.

Case 5: This 62 year old woman began to complain of pain in the posterior aspect of the neck in December, 1958. The pain radiated into both shoulders and became progressively more severe. She also complained of painful paresthesiae in the fingers of both hands. Weakness of the left upper limb appeared in January, 1959, and progressed to paralysis in one week. She was admitted to Montefiore Hospital on January 25th, where she presented a flaccid areflexic paralysis of the left upper extremity and a suggestive left Horner's symdrome. The right knee jerk was hyperactive and the right plantar response was equivocal. She was a very uncooperative subject and sensation could not be evaluated satisfactorily. Subjective complaints of pain and paresthesiae of the hands and fingers persisted, however. Lumbar puncture and manometrics, spinal fluid analysis and a myelogram were entirely normal. The hematocrit was 35 per cent. Other laboratory tests were normal.

The diagnosis was in doubt while neurological signs progressed. A diagnosis of myeloradiculopathy of unknown cause was suggested. On February 12th there was onset of paresthesiae and weakness of the left lower limb with absence of the left knee jerk. Within a few days urinary retention and flaccid paresis of the right upper limb appeared. By early March the patient presented flaccid areflexic paresis of both lower and the right upper limbs and flaccid areflexic paralysis of the left upper extremity. Plantar responses were described as flexor. Definite evidence of sensory loss was apparent in late February when impairment of position and vibratory sense was found in the hands. The patient's uncooperativeness hampered attempts at sensory evaluation throughout her course.

During the latter part of February the patient ran a febrile course without evidence of infection, and there was a progressive fall in the hematocrit associated with the appearance of immature leucocytes (myelocytes and promyelocytes) in the peripheral blood smear. Chest roentgenograms of March 5th disclosed a mass in the anterior mediastinum and many bizarre cells were found in a marrow aspirate. A tentative diagnosis of malignant lymphoma was made. Radiotherapy was directed to the mediastinum and a course of intravenous nitrogen mustard therapy was given. Following administration of nitrogen mustard the patient developed a pancytopenia, went into shock and expired on March 30th, 1959.

Examination of the general organs removed at autopsy revealed the presence of a malignant lymphoma (lymphosarcoma) which involved lymph nodes, kidneys, lungs and thyroid gland. The central nervous system was not examined. Of the peripheral nerves, only the left brachial plexus was removed. Grossly, it appeared normal. Microscopically, there was massive perineurial and interfascicular infiltration of nerve trunks by lymphosarcoma (Figure 8). Myelin sheaths and axons were destroyed or

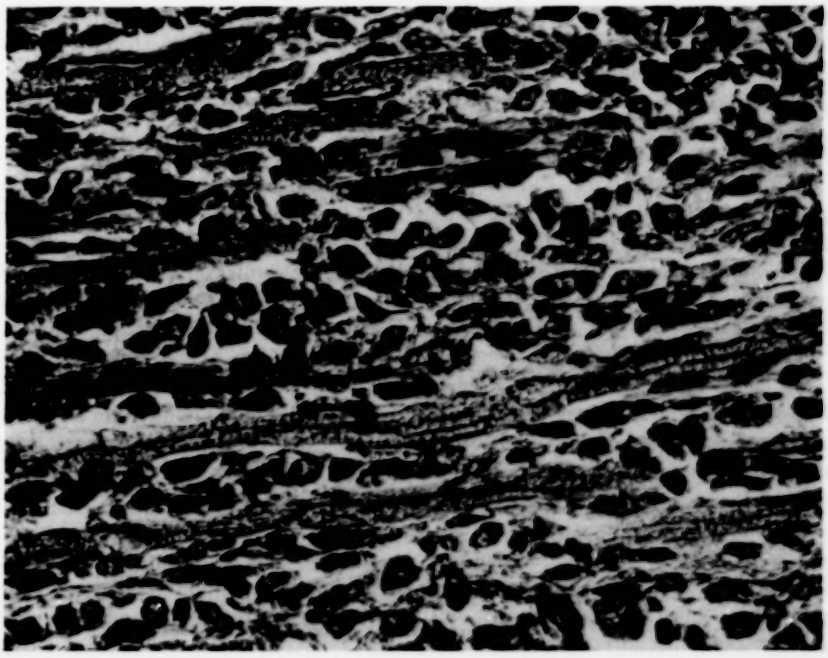

FIG. 8. Case 5. Lymphosarcoma in left brachial plexus. Hematoxylin-eosin stain. ×540.

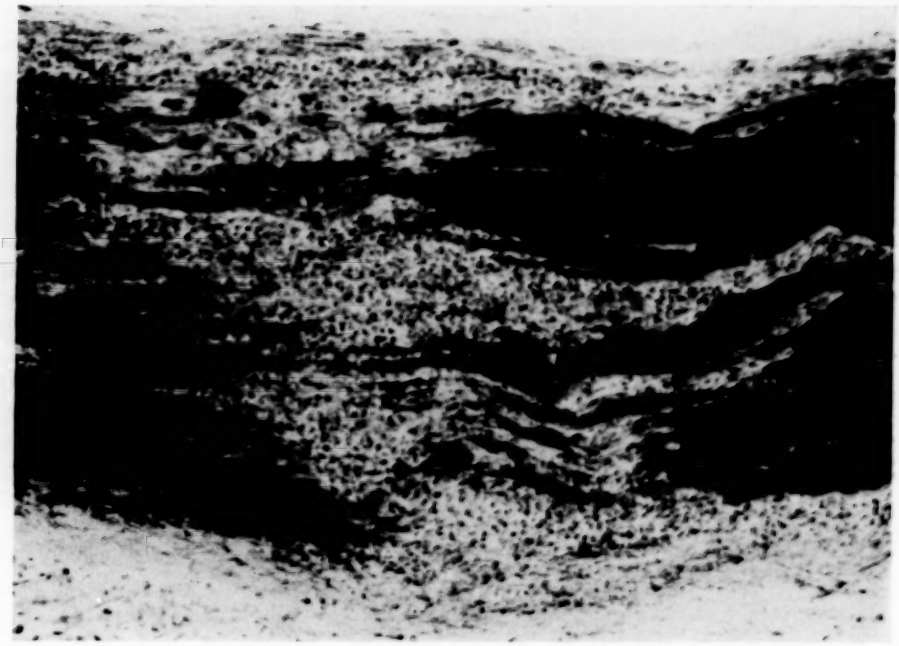

FIG. 9. Case 5. Tumor in brachial plexus. Spielmeyer stain. ×180.

presented severe pathologic alterations in sites of tumor cell infiltration (Figures 9, 10). There was abundant interfascicular sudanophilic material diffusely distributed in all sections, and there were axis cylinder and myelin sheath abnormalities in areas free of tumor infiltrates.

Case 6: A 50 year old white female was admitted to Montefiore Hospital on June 25th, 1955. For six months she had had pain and paresthesiae in the low back. The pain radiated down the posterior aspects of the thighs. For three months she had been aware of lack of sensation in the vagina and buttocks. Progressive weakness of the legs appeared one week before admission. The past history and functional inquiry were negative.

The patient had a temperature of 101°F., but general physical examination was otherwise normal. Pertinent neurologic findings included severe flaccid paraparesis without atrophy or fasciculation; absent Achilles reflexes and absent plantar responses; impaired vibratory and position sense in the toes with loss of superficial sensation in an S_{2-5} distribution; limitation of straight leg raising to 60° bilaterally.

Admission hemoglobin was 10.5 gm. per cent with a red blood cell count of 3.55 million. The white blood cell count was normal. The spinal fluid pressure was 100 mm. H_2O and the manometrics were open; the cell count was 12 lymphocytes per cu. mm., the protein value 241 mgm. per cent and the sugar 51 mgm. per cent.

The patient continued febrile and developed an atonic bladder. On July 7th she was disoriented. There was transient aphasia and right hemiplegia lasting less than 24 hours. Hepatosplenomegaly was noted on July 13th. At this time the red blood cell count was 2.75 million per cu. mm. and the hemoglobin was 8.5 gm. per cent. A peripheral blood smear showed many nucleated red cells, marked polychromatophilia and

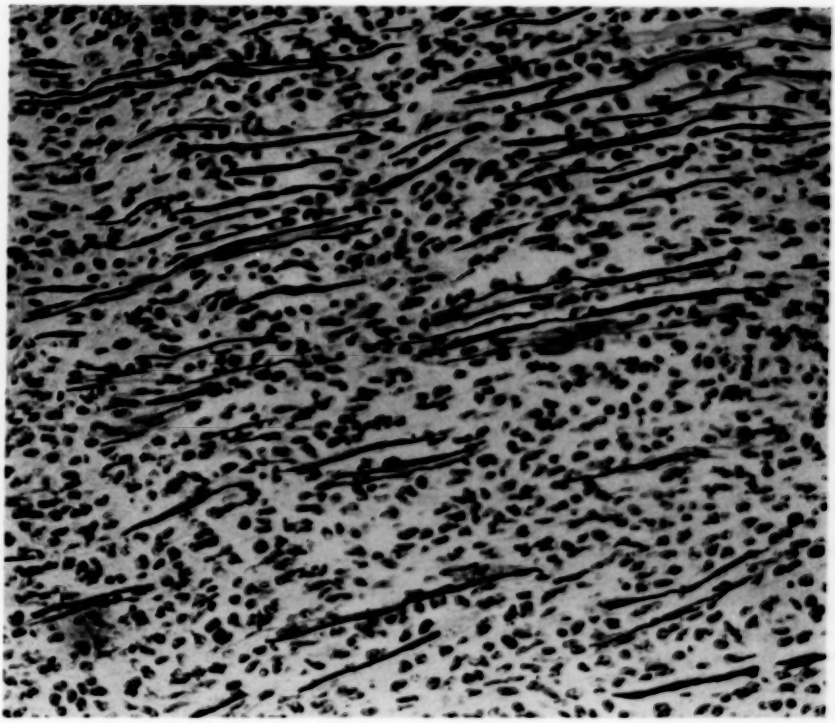

FIG. 10. Case 5. Same tumor in same plexus. Bielschowsky stain for axones. ×250.

spherocytosis, a shift to the left of the white cells to the promyelocyte level and an absence of platelets. On July 18th fever to 105°F. and shock developed, and the patient expired.

General autopsy findings are summarized as follows: erythremic myelosis (di Guglielmo's disease) involving the bone marrow and the spleen with erythroid infiltrates in the thyroid, lungs, liver, kidneys, and retroperitoneal tissues.

Grossly, the spinal cord was unremarkable save for chalky discoloration of the posterior columns at all levels. The left femoral, left median and right posterior tibial nerves were removed. They and the skeltal musculature were grossly normal.

The cerebral and spinal leptomeninges and the posterior spinal nerve roots were infiltrated by neoplastic elements of the erythroid series. The peripheral nerves showed a similar picture. There were both perineurial and interfascicular erythroid infiltrates, consisting predominantly of nucleated red blood cells (Figure 11). Spielmeyer and Sudan IV preparations confirmed the gross impression of ascending posterior column demyelination. The peripheral nerves disclosed mild to moderate diffuse demyelination. Foci of more severe demyelination were seen to be associated with infiltration by nucleated red blood cells. Mild diffuse and focal axis cylinder abnormalities were demonstrated in Bielschowsky preparations. The axonal changes were less severe than the myelin sheath alterations.

Case 7: In April, 1948, a 58 year old male developed progressive weakness of all extremities, but particularly of the lower limbs. Gradually he became unable to stand

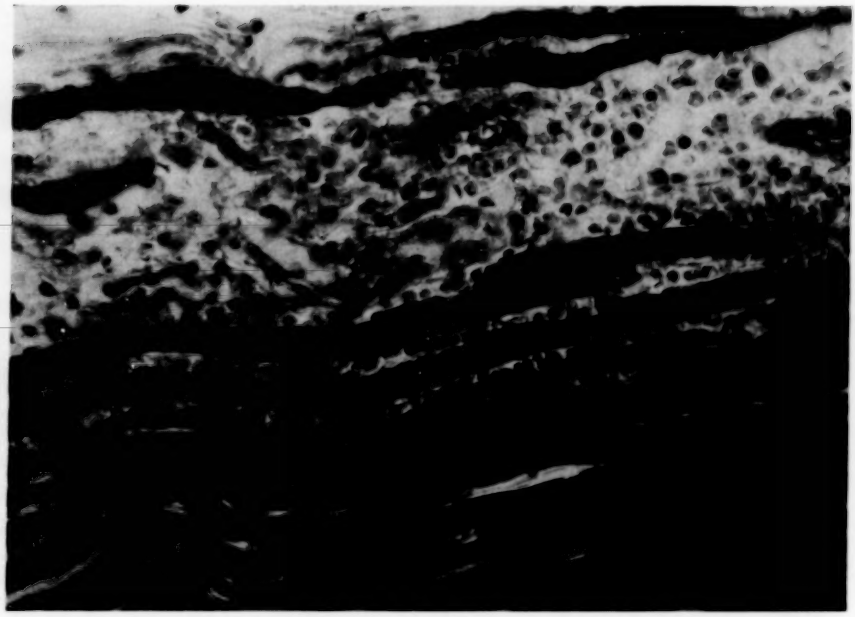

FIG. 11. Case 6. Interfascicular deposits of erythroid elements, some nucleated, in peripheral nerve with moderately advanced destruction of medullated fibers. Case of di Guglielmo's disease (erythromyelosis). Spielmeyer stain. ×400.

or walk. Pain in the arms and legs and back was a concomitant symptom. He was admitted to Montefiore Hospital June 14th, 1948. The past history disclosed that laparotomy had been performed in 1946 for abdominal pain and a retroperitoneal mass had been found. A diagnosis of lymphosarcoma had been made on histologic examination of a biopsy specimen. The patient could "barely move" the lower limbs and the arms were diffusely paretic. Muscular wasting was generalized but particularly severe in the calves, thighs and intrinsic hand muscles. Tendon reflexes were absent in the lower limbs and barely obtainable in the arms. Position sense was lost in the toes and impaired in the fingers. Vibratory sense was lost to the costal margins. Poorly delimited zones of hypesthesia and hypalgesia were noted in the arms and legs.

Laboratory investigations, including radiographs of the spine, were negative except for a moderate anemia. Lumbar puncture was not performed.

A diagnosis of "Guillain-Barre syndrome" was entertained. Inanition progressed and he became febrile and lapsed into coma before death on August 28th, 1948. Neither nuchal rigidity nor cranial nerve palsies were noted at any time.

Postmortem examination disclosed the presence of a malignant lymphoma (Hodgkin's sarcoma) involving peri-aortic tissue and the brain.

The spinal cord, the spinal meninges and the nerve roots of the cauda equina were unremarkable grossly. Of the peripheral nerves, only the femoral nerve was removed. It, too, had a normal macroscopic appearance. Microscopic examination of the spinal and cerebral leptomeninges disclosed diffuse invasion by lymphoma cells. There were hematoxylin-eosin sections of the spinal nerve roots and the nerve roots of the cauda equina, as well as of the femoral nerves. These showed perineurial and interfascicular aggregations of lymphoma cells (Figures 12, 13). Focal demyelination and axis

FIG. 12. Case 7. Hodgkin's sarcoma in sheath of peripheral nerve. Note ballooning in degenerating myelin sheaths. Hematoxylin-eosin stain. ×400.

cylinder destruction were found in areas of tumor cell infiltration. There was also diffuse abnormality of myelin sheaths and axons. In Nissl preparations of the spinal cord the neurones of the anterior horns showed axonal change. The posterior columns were demyelinated.

Case 8: The patient, a white male, was admitted to Montefiore Hospital on February 5th, 1958, at age 53. In 1953, surgical biopsy and histologic examination of an enlarged cervical lymph node had resulted in a diagnosis of lymphosarcoma. In 1957, hematologic evidence of subacute lymphatic leukemia appeared. Thereafter the patient's course was one of relentless progression. Death on March 26th, 1958 resulted from hemorrhage and infection secondary to thrombocytopenia, anemia and granulocytopenia. No definite abnormalities were recorded in the cursory neurological examinations performed during the last months of life nor was note made of any neurological symptomatology.

Examination of tissues removed at autopsy resulted in a diagnosis of chronic lymphatic leukemia involving lymph nodes, bone marrow, liver, spleen, adrenal glands, kidneys and gastrointestinal tract. There were focal pneumonitis and generalized arteriosclerosis. Petechiae were found in the renal pelves, peritoneum and endocardium.

Except for a small nodule of leukemic tissue in the falx cerebri, the brain and spinal cord were normal grossly. Both brachial plexuses and both sciatic nerves were removed. On macroscopic examination these were found to be enlarged and had a dark brown coloration. Their cut surfaces presented a granular appearance. Histologic examination of these nerves disclosed massive perineurial infiltration by leukemic cells. There were also large interfascicular infiltrates of tumor cells (Figure 14). Intensive focal demyelination was found in areas of interfascicular infiltration by tumor, while axis cylinders, though abnormal, were less severely affected. There was

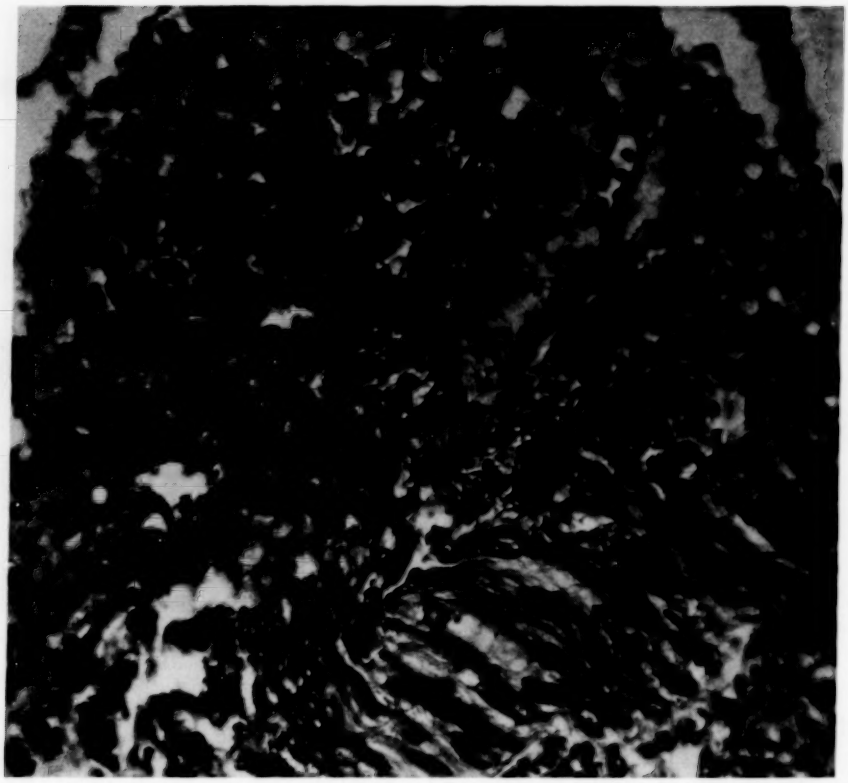

FIG. 13. Case 7. Hodgkin's sarcoma infiltration in cauda equina root. Hematoxylin-eosin stain. ×400.

diffuse mild to moderate abnormality of myelin sheaths and axis cylinders in segments of nerve uninvolved by focal metastases. Hematoxylin-eosin preparations of the spinal cord were normal.

CASE REPORTS: GROUP 2

CARCINOMATOUS INFILTRATES IN CRANIAL AND SPINAL NERVES

Case 9: This was a 60 year old female whose final admission to Montefiore Hospital was on June 1st, 1956. A diagnosis of carcinoma of the left breast with metastases to axillary lymph nodes and bone had been made in 1952. In May, 1956, signs of a lesion of the left brachial plexus appeared and progressed to total paralysis and anesthesia of the left upper limb. She died in February, 1957, as a result of inanition and diffuse pulmonary metastases.

The presence of an anaplastic carcinoma of the left breast was confirmed at autopsy. There were metastases to the lungs, bones, brain and left brachial plexus. The last named structure was firm to palpation and obviously infiltrated by tumor. Microscopic examination disclosed extensive neoplastic deposits in the perineurial lymphatics of some nerve fiber bundles which were compressed in consequence (Figure 15). Other nerve bundles were invaded and replaced by tumor cells. Spielmeyer and Sudan IV stains showed severe demyelination and large amounts of sudanophilic material.

Case 10: A 61 year old patient underwent

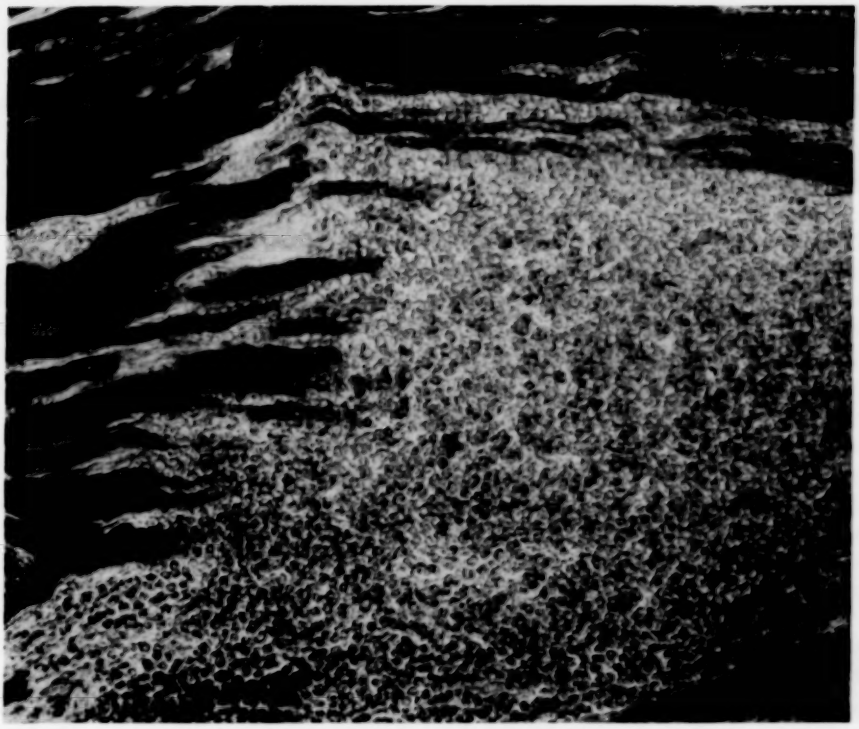

FIG. 14. Case 8. Massive leukemic (lymphatic) infiltrate in left brachial nerve. Spielmeyer stain. ×250.

FIG. 15. Case 9. Metastatic carcinoma of breast in brachial plexus. Note sheets of tumor cells in perineurial lymphatics and between individual nerve fasciculi. Hematoxylin-eosin stain. ×30.

prostatectomy and orchiectomy in 1953 for carcinoma of the prostate. In March, 1955, he noted persistent dull pain in the right shoulder, slowly progressive weakness and atrophy of the proximal musculature of the right upper limb and a feeling of "numbness" in the outer aspect of the right upper arm. Cervical spine films showed a destructive lesion of the body of C5. In September, 1956, pain, weakness, atrophy and numbness appeared on the left, in a similar distribution. Symptoms were slowly progressive. There was never a complaint of radicular pain and discomfort in the neck was minimal and present early in the course only. The patient was admitted to Montefiore Hospital on March 7th, 1956, when neurologic examination demonstrated atrophy and paresis of both deltoid and both biceps muscles. The pectoralis major and serratus anterior muscles were less severely involved. The triceps muscle and the dorsiflexors of the wrist were weak on the right. The tendon reflexes were absent in the upper extremities and there was hypalgesia and hypesthesia in the distribution of dermatomes C4 to C6 bilaterally. Death occurred on March 26th, 1956, from obstructive uropathy with hematuria, azotemia, intractable urinary infection and bronchopneumonia.

Necropsy diagnoses were as follows: scars of suprapubic prostatectomy and bilateral orchiectomy for carcinoma of the prostate; metastases to cervical vertebrae; necrotizing ureteritis and pyelitis; acute pyelonephritis; confluent bronchopneumonia; adenocarcinoma in adenomatous rectal polyp with metastases to the liver.

Macroscopic examination of the spinal cord revealed a small zone of epidural metastasis which did not compress the cord. The spinal nerve roots from C6 to T1 were removed on the right side together with brachial plexus and the ulnar nerves. The cervical roots on the left side were not examined. C6 and C7 nerve roots were surrounded by firm granular neoplasm distal to their point of issuance from the intervertebral foramina. Microscopic examination disclosed compression and infiltration of these roots by metastatic carcinoma of the prostate. The tumor was both perineurial and interfascicular in location. Spielmeyer and Sudan IV stains demonstrated severe demyelination of the involved roots. The ulnar nerve was the site of mild demyelination. Axis cylinder stains of the ulnar nerve and posterior cervical spinal roots were abnormal. The cervical posterior root ganglia were normally populated. However, there was ascending degeneration of the posterior columns of the spinal cord bilaterally, which was confined to the cuneate fasciculi.

Case 11: A 71 year old male was admitted to Montefiore Hospital on October 25th, 1955, and expired on November 9th, 1955. One year before admission progressive dyspnea developed and a chest roentgenogram revealed the presence of a left hilar mass. A diagnosis of bronchogenic carcinoma was made. For two months his voice had been hoarse and his gait unsteady. During the several weeks before admission proptosis of the right eye, weakness of the right side of the face and right-sided deafness were noted.

On examination he was dyspneic and cachectic and had signs of a left pleural effusion. The neck was supple. There was a suggestive proptosis of the right eye. Abnormal neurologic signs included hoarse slurred speech; ataxia of gait; symmetrical hyperreflexia; bilateral Babinski signs; ptosis of the left eyelid; absence of the right corneal reflex; peripheral-type paralysis of the right facial masculature; diminished hearing on the right.

Spinal fluid manometrics were normal but the total protein was 172 mgm. per cent and the sugar 28 mgm. per cent. The spinal fluid cell count was zero.

The patient became confused, stuporous and doubly incontinent before death.

Anatomical findings at necropsy included an epidermoid carcinoma of the left lung

with metastases to lymph nodes, pleura, adrenal glands and brain. The cerebral leptomeninges at the base of the brain and overlying the cerebellum were diffusely opacified by a thin layer of gray, granular material. The right 7th and 8th cranial nerves were of normal size. The right 5th nerve was enlarged to a diameter of 0.5 cm. Microscopic examination revealed extensive leptomeningeal carcinomatosis. The 3rd, 5th, 7th, and 8th cranial nerves were invaded by tumor cells which lay between nerve fascicles or replaced large portions of the nerve. Spielmeyer and Sudan IV stains of the involved nerves showed extensive demyelination and the presence of large amounts of sudanophilic material in and between nerve fascicles.

Case 12: A 64 year old male developed a bloody discharge from the right nostril in November, 1955. In April, 1956, a resection of a carcinoma of the right antrum was performed. The patient complained of numbness of the left side of the face and diplopia on looking to the left in July. Subsequent examinations disclosed the following neurological abnormalities: fixed pupils; analgesia in the distribution of the 1st and 2nd divisions of the left 5th nerve; left lateral rectus muscle paralysis; absent caloric responses on the left; marked dysarthria and absence of the gag reflex on the left; paresis of the right lower limb with increased tendon reflexes and impairment of position and vibratory sense in the right toes. Skull roentgenograms disclosed erosion of the roof of the right antrum. The spinal fluid protein was 83 mgm. per cent but the cell count was zero and the spinal fluid sugar was normal. Death occurred on October 20th, 1957.

At autopsy an anaplastic epidermoid carcinoma of the right maxillary sinus was found which had eroded the base of the skull and spread extensively in the cerebral and spinal leptomeninges. Multiple cranial nerves and spinal nerve roots were infiltrated by carcinoma cells and there was associated demyelination of a severe degree (Figure 16).

Case 13: A 62 year old woman was admitted to Montefiore Hospital in August, 1955. In 1951 a left radical mastectomy was done for an anaplastic carcinoma of the breast. Cervical adenopathy developed in 1953. In February, 1955, shooting pain in a C_5 distribution developed on the right. Similar pain followed on the left side and was associated with paresis of both upper limbs. Neurologic examination three days after admission disclosed marked wasting and weakness of both deltoid and both biceps muscles. Both triceps muscles were slightly paretic. Tendon reflexes were absent in the upper extremities. There was no demonstrable sensory loss. Radiographic examination of the spine showed widespread metastases. The bodies of vertebrae C_3, C_4 and C_5 were compressed and misalligned as a result of osteolytic metastases. On December 1st, 1955, signs of spinal cord compression appeared. Death occurred on December 28th, 1955, from a combination of urinary and pulmonary infection. Sensory loss was never demonstrable.

General autopsy findings included metastasis by a carcinoma of the breast to bone, lung, liver, lymph nodes and cerebral and spinal dura. There was focal pneumonia with abscess formation and chronic cystitis and bilateral acute pyelonephritis. The metastasis to the cervical dura measured 5 cm. in length and the cervical nerve roots passed directly through the neoplastic mass. Histologic examination revealed that the tumor had penetrated the dura and invaded leptomeninges and nerve roots. Groups of tumor cells lay within nerve root fascicles.

Case 14: A 37 year old man noted a swelling of the right upper neck in 1952. Punch biopsy of the nasopharynx disclosed an anaplastic epidermoid carcinoma in 1953. In March, 1957, diplopia developed and complete neurologic examination disclosed only isolated paralysis of the right abducens

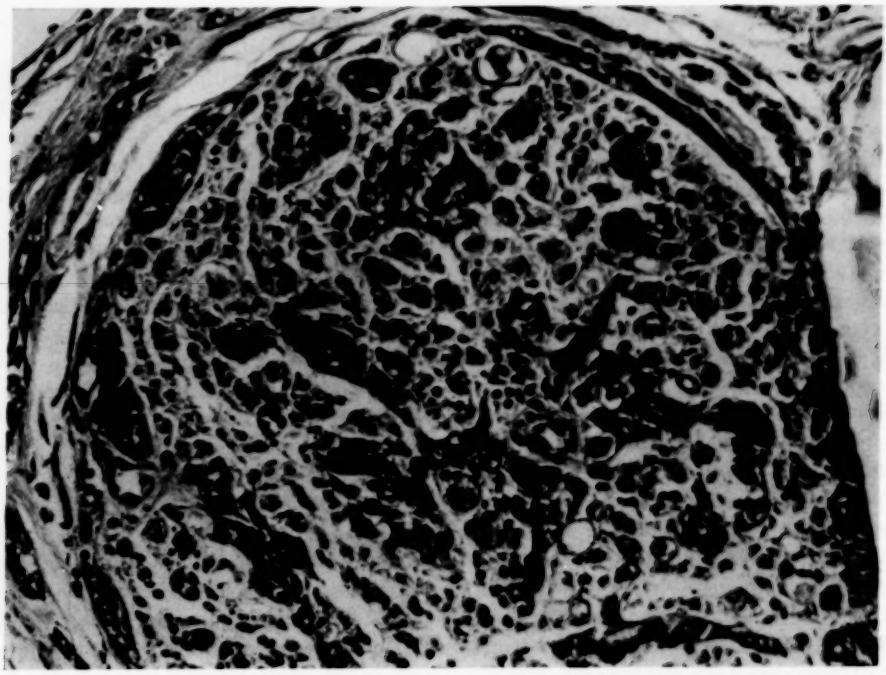

FIG. 16. Case 12. Anaplastic epidermoid carcinoma of antrum infiltrating posterior spinal nerve root. Hematoxylin-eosin stain. ×250.

FIG. 17. Case 14. Carcinoma of the nasopharynx with infiltration of 6th cranial nerve. Note severe destruction of myelin sheaths. Spielmeyer stain. ×400.

nerve. No further neurologic signs appeared prior to death on October 11th, 1957.

At autopsy the presence of an anaplastic nasopharyngeal carcinoma was confirmed. The brain was entirely normal. The cranial nerves were individually identified and examined and did not display macroscopic abnormality. However, histologic sections of the right 6th cranial nerve demonstrated infiltration by carcinoma cells (Figure 17). Demyelination of those nerve fibers adjacent to neoplastic infiltrates was evident in Spielmeyer preparations. Curiously, there was no sudanophilic material in the involved nerve, despite severe demyelination of some fibers. The cerebral and spinal leptomeninges did not contain any metastases.

DISCUSSION

The cases of importance to this discussion are those described in Group 1. The examples of neuropathy included in Group 2 were chosen merely to illustrate, even more conclusively, that neoplastic infiltration of nerves may be accompanied by demyelination of contiguous nerve fibers.

A clinical syndrome of symmetric sensorimotor polyneuropathy was present in five cases of Group 1 at some time during the course of the illness. Of the three cases remaining, there were no symptoms which could be related definitely to peripheral neuropathy in two (Cases 3 and 8), while in one (Case 6), the syndrome was that of a cauda equina lesion. Atypical features among the patients presenting a symmetric polyneuropathy at some time in their courses included dementia in Case 2, onset with monoplegia in Case 5 and the presence of leptomeningeal infiltrations in Case 7. The atypical features of the clinical symptomotology in some of our cases do not alter the conclusions that: 1) perineural and interfascicular metastases occurring in multiple myeloma, malignant lymphoma and allied disorders are regularly attended by focal demyelinating lesions with propagation of demyelination beyond the site of focal involvement; 2) such metastases may be numerous and may involve the peripheral nerves of all the extremities; 3) the peripheral nerve lesions may be unaccompanied by clinical or anatomical evidence of metastases to the leptomeninges or cranial nerves; 4) a clinical syndrome of symmetric sensorimotor polyneuropathy may attend multiple metastasis to the peripheral portion of the nervous system; 5) this syndrome may be indistinguishable from that described in association with some cases of malignant lymphoma, multiple myeloma and carcinoma, and ascribed to a "metabolic" etiology. We do not wish to imply that the mechanism responsible for neuropathy in our cases is necessarily applicable to the problem of "carcinomatous" neuropathy described by Denny-Brown and others. Further, cases of polyneuropathy with thorough anatomical study have been described in detail in multiple myeloma and malignant lymphoma in the absence of metastases to the peripheral nerves. However, the findings described in our material would indicate that careful anatomical study of the peripheral nerves is indicated in polyneuropathy accompanying multiple myeloma, malignant lymphoma and such allied disorders as erythroleukemia and erythremic myelosis before a "metabolic" pathogenesis is considered.

Cases 1 to 3, in which the primary neoplasm was a multiple myeloma, are of particular importance, since disseminated metastases to peripheral nerves have not been described previously in this condition. Brief mention of myelomatous involvement of the sciatic nerve in one patient was made by Brownell (3). He did not provide detailed clinical correlation. Other authors have described the association of polyneuropathy with metastatic involvement of multiple peripheral nerves in leukemia (1, 10) but have denied the metastases any role in the genesis of the clinical signs of polyneuropathy and anatomical findings of demyelina-

tion, preferring to ascribe these to a "toxic" etiology.

Mention may also be made of accounts in the literature attributing polyneuropathy accompanying myeloma to the compression of peripheral nerves by amyloid infiltration of endoneurium and perineurium. To our knowledge such amyloid deposits have not been demonstrated anatomically and their occurrence, though widely quoted in the literature (4, 8, 15), remains pure conjecture. The finding of amyloidosis in other organs, as in the case of Dumas *et al.* cannot be used to postulate similar involvement of neural structures. In Case 1 of the present series generalized amyloidosis was unaccompanied by amyloid infiltration of any part of the nervous system.

Finally, the occurrence of remissions of symptoms, as in Cases 1 and 4 and possibly Case 2, may be commented upon. In these cases a relative sparing of axons in areas of tumor infiltration was a conspicuous finding, and suggests the possibility of restitution of function with spontaneous or therapeutically induced regression of the neoplasm. A remarkable improvement in symptoms in Case 4 was temporally related to signs of regression of the primary neoplasm under therapy.

SUMMARY

Two groups of cases are described in which degeneration of myelin sheaths and axones of cranial, spinal and/or peripheral nerves was associated with infiltration of these structures by malignant tumor cells.

In the first group of eight cases, five had an associated clinical syndrome of symmetric sensorimotor polyneuropathy. Where sufficient anatomic material was available, numerous metastases were found in the peripheral nerves of the extremities. At the sites of metastatic infiltration, there was focal degeneration of myelin sheaths and axones. Usually, axones were less severely degenerated. Segments of nerve free of metastases showed mild or moderate demyelination which was believed to represent Wallerian degeneration originating at sites of focal tumor infiltration. The primary neoplasms in cases of this first group included multiple myeloma, malignant lymphoma, erythroleukemia and erythremic myelosis.

The second group comprised examples of infiltration of cranial nerves, spinal nerve roots and nerve plexuses by metastatic epithelial neoplasms. In these cases, too, infiltration of neural structures was associated with degenerative changes in myelin and axones at the sites of tumor invasion.

It is concluded that the clinical picture of neuropathy and the anatomic findings of degenerative changes in nerve fibers were the direct result of the tumor infiltrations and that, in the cases presented in this paper, the postulation of a "metabolic" or "toxic" pathogenesis for the neuropathy is not warranted. It would appear that, in cases of polyneuropathy accompanying multiple myeloma, malignant lymphoma and allied disorders, careful examination of the peripheral nerves should be made to establish the presence or absence of metastatic infiltrations.

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STUDIES IN PARKINSONISM: RELATIONSHIPS BETWEEN TONE AND TREMOR IN PARKINSONISM AND IN NORMALS

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INTRODUCTION

Although the clinical symptomatology of tone and tremor in Parkinsonism has been described thoroughly for almost 200 years, the relationship between these two phenomena has been the subject of much controversy. The purpose of the present study is to determine the correlation between tone and tremor in the patient with Parkinsonism and to what extent this relationship obtains in normals.

The first suggestion was made by Hughlings Jackson in 1896 when he considered "tremors as rigidity spread out thin and rigidity as tremors run together" (8). This Jacksonian concept was based on clinical observation. The foremost opposing opinion is that of F. M. R. Walshe (12), who, on the basis of experimental work of his own and others, states that rigidity and tremor are separate phenomena, without fundamental relationship. Walshe found that by infiltrating the muscles of the Parkinsonian patient with 1 per cent procaine, rigidity was abolished, but tremor persisted. He also cited the work of Liljestrand and Magnus (7), which showed that although a muscle was flaccid from procaine infiltration, it would still respond to tonic neck reflexes. From this Walshe concluded that the rigidity of Parkinsonism is a true proprioceptive reflex. Walshe believes that tremor is based on an entirely different mechanism, basically the result of the emergence of a normal cortical rhythm through a defect in lower level mechanisms. Thus in his opinion, cortical activity is an essential condition of tremor, but not of rigidity. On the other hand an intact proprioceptive arc is essential for rigidity but not for tremor. Pollock and Davis (9) sectioned the dorsal roots of an extremity of a Parkinsonian patient with rigidity and tremor. Flaccidity resulted but tremor was not abolished, although altered in amplitude, rate and rhythm.

Hoefer (6) using intramuscular electromyography, showed that the resting rigid muscle manifests continuous low grade action potential activity. When tremor appeared in the same extremity the low grade activity became augmented, corresponding to the observed motion. The result was bursts of action potentials corresponding to tremor, superimposed upon the low grade background activty of rigidity. This finding, according to Hoefer, supports Jackson's theory.

Browder and Rabiner (3) found support, in their opinion, for Jackson's theory from a surgical case in which a patient with severe rigidity was subjected to surgical section of the anterior limb of the internal capsule. When the latter was transected 2 cm. rostral to the genu, rigidity ceased, but was replaced by tremor. Futher sectioning stopped the tremor. They state that tone and tremor are essentially the same phenomenon but appear differentially due to temporal spacing of their components. In their opinion, when tremor becomes sufficiently rapid, rigidity results; as rigidity lessens, tremor appears.

Recent animal experimentation suggests that some of the neural circuits responsible for tremor and rigidity are anatomically allied in the reticular formation of the brain stem (5). The physiologic relationships have not yet been clarified.

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METHODS

DEFINITION OF TERMS

The methodology for the quantitation of tone and tremor has been described in previous reports (2, 4, 11). The methods utilize electronic techniques which, in our opinion, provide the most accurate means to date for recording and quantitating tone and tremor.

Tone is defined as a continued state of tension in a muscle (10). This tension is quantitated in terms of dyne-cm. of torque. For the measurement of muscle tension in the upper extremities, the patient is seated at the tonometer, which consists of a movable metal arm driven to and fro through a constant arc by an electronically controlled motor. The patient places his upper limb on the tone arm and relaxes completely. Any resistance to the motion of the arm, *i.e.*, muscle tension, is transmitted to strain gauges mounted beneath the moving arm. The strain gauges are arranged in the form of a Wheatstone bridge, distortion of which produces a microvoltage output. After suitable amplification, this signal is written out by a direct-writing oscillograph. The deflection of the pen from the baseline is proportional to the instantaneous torque (muscle tension). By means of a calibration graph these measurements are converted into absolute physical units. Both right and left upper extremities are measured for ten trials so that the mean torque values of extension and flexion (in megadyne-centimeters) for both upper limbs constitute the four parameters of muscle tone. Thus, by means of carefully controlled conditions of measurement, utilizing electronic principles, the physiologic variable of muscle tone is quantitated in absolute physical units.

Tremor is measured by means of a variable reluctance accelerometer which was first used for this purpose by Agate *et al.* (1). This accelerometer is the first part of the tremor detecting system and serves to sense the tremor. The second portion of the system is a console composed of electronic equipment to amplify the signal from the accelerometer. The final unit which does the actual recording is a converted standard Offner 6-channel EEG[2]. The accelerometer used is a Glennite AVR-250[3]. This accelerometer, which weighs 2.5 grams, is designed to measure the low frequency vibrations and accelerations on small structures. The accelerometer is a variable reluctance pickup, housing two active inductive bridge arms. Each inductive arm is wound with a magnetic shield provided with an air gap, and a suspended magnetic armature controls the air gaps in accordance with the applied acceleration. The accelerometer is designed for use with standard carrier systems (1500 to 5000 cycles per second). The inductive windings of these instruments form two bridge arms; the other arms are included in this carrier equipment. The accelerometer has a sensitivity of 1.07 millivolts/G. A console houses the necessary equipment to balance and calibrate the bridge, a carrier oscillator, an input amplifier, a phase splitter, a push-pull amplifier, a phase sensitive demodulator and an input coupler. The write-out unit is a standard EEG galvanometer. Special sensitivity controls are built into the unit and other modifications are necessary to achieve the special clarity desired. The equipment, including circuit and operational descriptions, is presented in previous reports. Tremor of Parkinsonism has been shown to be composed of seven parameters. These have been described in previous reports: 1) harmonic wave-forms, 2) spindle formation, 3) abrupt wave-form changes (regular to irregular and vice versa), 4) periodicity in the wave-form amplitude, 5) a greater than normal incidence of regular frequency, 6) amplitude, 7) an actual frequency, which ranges between 4.2 and 6.2 cycles per second in the Parkinsonian patient. The range in normals is between 6.2 and 8.8 cycles per second.

[2] Manufactured by Offner Electronics, Inc., Chicago, Illinois.

[3] Manufactured by Gulton Industries, Inc., Metuchen, New Jersey.

MATERIAL

Twenty-five patients with the clinical syndrome of Parkinsonism were selected at random. All patients were off anti-Parkinsonian medication for at least 24 hours prior to recording. The results of measurement of tone and tremor in these patients as well as in normals have been previously reported (2, 4, 11).

The control series consisted of 18 persons with no neurologic disease, selected at random from the general population. The ages of the control series correspond to those of the Parkinsonian series.

RESULTS

Table 1 contains the basic data on the Parkinsonian patients included in the series with a clinical evaluation of tremor in all extremities, head and tongue, and tone in the upper extremities. Tremor was evaluated subjectively by one author and tone by an-

TABLE 1

Basic Data of Parkinsonian Series

Pt.	Age (yrs.)	Sex	Etiol.	Dur. (yrs.)	Days off Rx	Clinical Evaluation							
						Resting Tremor						Tone	
						R.U.E.	L.U.E.	R.I.E.	L.L.E.	Head	Tongue	R.U.E.	L.U.E.
1. N.A.	39	F	E	2	7	½	0	0	0	0	0	2	1
2. D.B.	55	M	E	20	1	2	1	0	1	1	1	4	4
3. G.C.	40	M	E	22	1	0	0	0	0	0	1	0	0
4. T.C.	73	M	A	4	21	0	0	0	0	0	1	1	0
5. W.C.	58	M	I	6	6	0	0	0	0	0	0	1	2
6. J.F.	58	M	E	31	6	0	2	0	1	1	2	1	3
7. L.G.	45	F	E	21	2	½	2	0	0	0	0	1	3
8. N.G.	68	M	E	8	6	0	0	0	0	0	1	2	2
9. A.H.	56	M	I	1	3	½	0	0	0	0	0	0	0
10. G.H.	38	F	E	10	3	½	1	1	1½	0	½	2	1
11. J.L.	63	M	I	5	7	1	1	0	0	0	½	1	2
12. L.M.	65	M	I	1	N.O.	1	2	0	0	0	0	1	0
13. M.M.	57	F	E	8	7	1	2	½	1	½	0	0	1
14. T.M.	62	M	E	30	7	1	½	0	0	0	1	1	1
15. M.M.	57	M	E	6	6	3	2	2	1	1	1	1	0
16. L.N.	63	M	A	2	6	0	0	0	0	0	1	2	3
17. O.O.	68	F	A	2	7	2	2	2	1	0	1	1	3
18. J.O.	64	M	A	3	5	3	1	0	0	0	0	4	4
19. M.O.	69	F	A	2	7	0	2	0	0	0	0	0	1
20. E.P.	56	M	CO-P	2½	N.O.	½	0	0	0	0	0	1	0
21. J.R.	73	M	A	5	7	1	3	0	0	0	1	1	1
22. H.R.	55	F	E	5	3	0	0	0	2	0	½	0	0
23. E.S.	69	F	A	3½	3	1	1	0	0	0	2	0	0
24. M.V.	62	F	A	2	3	0	0	0	0	0	0	1	0
25. H.W.	72	M	A	2	1	1	½	0	0	0	0	1	0

Key to Symbols:

Etiol. = Etiology
Dur. = Duration of symptoms in years
R.U.E. = Right upper extremity
R.L.E. = Right lower extremity
L.U.E. = Left upper extremity
L.L.E. = Left lower extremity
M = Male F = Female
E = Post-encephalitic, A = Arteriosclerotic, I = Idiopathic, CO-P = Carbon monoxide poisoning.
N.O. = Never on medication

Tone-Tremor grading (gross clinical):
1 = Mild
2 = Moderate
3 = Severe
4 = Very severe

other, independently and without the knowledge of the other's judgment.

Table 2 contains the data for correlation of tone and tremor. The torque values listed in column 1 are correlated by means of product moment correlation coefficients with each of the parameters of tremor also shown in Table 2. Torque values are expressed in megadyne-cm. and tremor values are expressed in per cent of occurrence of the parameter in the total number of trials per patient.

The results of the study may be divided into the correlation of tone and tremor by 1) objective (electronic) methods and 2) subjective evaluation. The subjective method pertains only to Parkinsonian patients since tone and tremor measurements by this means were normal in the control group. The objective methods concern (a) the normal control group and (b) the Parkinsonian group.

CORRELATION OF TONE AND TREMOR BY OBJECTIVE MEANS

Table 3 shows the product moment correlation coefficients (r value) between the torque values and the various parameters of tremor in Parkinsonism. The product moment correlation coefficients may theoretically have any value ranging from -1 to $+1$. The former is perfect inverse correlation and the latter perfect direct correlation. A value approaching 0 indicates that the two measures are not correlated. The r values in Table 3 range from 0.33 to 0.68. All values except amplitude periodicity show a significant degree of correlation ($p = <0.05$) as can be seen from Table 3. The parameter of amplitude periodicity closely approaches such significance ($p = 0.06$). Especially noteworthy is the relationship of harmonics and spindles to hypertonus. All r values except frequency in cycles per second are positive. This indicates a direct correlation between hypertonus and regular frequency, regular amplitude, incidence of amplitude periodicity, abrupt wave-form change, har-

TABLE 2

Parkinsonian Tremor Parameters Correlated with Torque Values

Patient	Torque megadyne-Cm. (I)	Frequency Regularity (II) %	Amplitude Regularity (III) %	Frequency c/sec. (IV)	Amplitude Periodicity (V) %	Abrupt wave form change (VI) %	Harmonics (VII) %	Spindles (VIII) %
1. N.A.	1.85	49	41	7.6	0	5	0	5
2. D.B.	8.45	73	65	5.6	0	0	7	18
3. G.C.	2.00	0	0	7.4	0	0	0	0
4. T.C.	1.60	11	0	7.6	0	0	1	0
5. W.C.	4.50	0	2	8.4	0	0	0	2
6. J.Fo.	7.05	71	29	6.0	0	0	39	39
7. L.G.	2.05	65	55	5.5	23	8	9	10
8. N.G.	1.00	0	0	8.3	0	0	0	0
9. A.H.	2.00	42	24	7.5	0	0	0	26
10. G.H.	5.05	89	78	6.0	6	3	7	11
11. J.L.	3.50	47	17	6.4	0	0	0	25
12. L.M.	1.60	43	22	6.2	7	1	26	6
13. M.Ma.	3.60	95	93	4.9	30	0	11	20
14. T.McH.	5.03	61	18	8.1	0	1	0	33
15. M.Mo.	4.85	100	89	4.2	50	0	56	22
16. L.N.	1.05	0	0	8.6	0	0	0	0
17. O.O.	2.35	100	100	5.4	68	0	7	11
18. J.O.	5.90	86	79	5.9	59	11	5	9
19. M.O.	4.80	48	52	5.1	50	0	13	0
20. E.P.	2.70	7	0	8.2	0	0	0	0
21. J.R.	6.80	82	68	5.2	60	16	47	23
22. H.R.	3.05	55	9	6.9	0	0	6	19
23. E.S.	4.05	30	0	7.5	0	8	0	25
24. M.V.C.	1.45	0	0	7.6	0	0	0	0
25. H.W.	5.75	40	6	7.1	26	8	15	6

TABLE 3

*Parkinsonian Tremor Parameters Correlated with Torque Values**

Parameter	r	Z_r	p
Frequency regularity	0.49	0.54	0.0060
Amplitude regularity	0.41	0.43	0.0244
Frequency	0.45	0.49	0.0122
Amplitude periodicity	0.33	0.34	0.0591
Abrupt wave-form change	0.35	0.36	0.0505
Harmonics	0.68	0.82	<0.0013
Spindles	0.52	0.58	0.0049

* The r values represent the Pearson product moment correlation coefficient. These r values were transformed according to the Fisher logarithmic method and referred to a normal probability table.

$$Z = \frac{1}{2} \log_e \frac{1 + r}{1 - r}$$

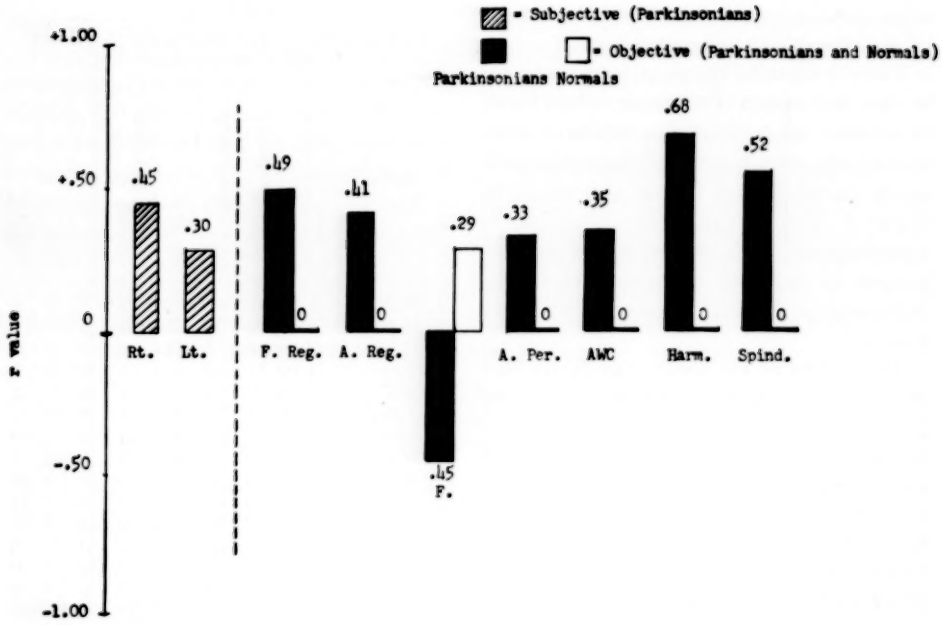

FIG. 1. Correlation of tone (torque values) and tremor parameters.
Key: Rt. = Right; Lt. = Left; A. = Amplitude; Reg. = Regularity; Per. = Periodicity; AWC = Abrupt Wave Form Change; Harm. = Harmonics; Spind. = Spindles.

TABLE 4
Correlation of Torque and Tremor Frequency in the Normal Series

Patient	Torque of Flexion Left Arm (dyne-cm. × 10^6)	Tremor Frequency (cycles per sec.)
1. J. Bal.	1.20	6.7
2. J. Bas.	.50	8.3
3. M.B.	1.40	6.9
4. R.B.	1.00	7.5
5. J.DeB.	1.60	8.2
6. L.E.	.85	8.6
7. A.G.	3.90	8.8
8. M.K.	3.20	7.7
9. E.L.	.90	6.6
10. E.McC.	.55	8.2
11. W.M.	1.05	8.6
12. W.McK.	.85	8.2
13. M.P.	2.65	8.7
14. A.R.	1.80	8.6
15. M.T.	.80	7.5
16. R.T.	3.25	7.9
17. G.W.	.15	7.6
18. C.Z.	3.00	8.0

$r = +0.29$ $z_r = 0.30$ $p = 0.85$.

monics, and spindles (see Figure 1). The relationship between hypertonus and frequency of tremor in cycles per second is a reciprocal one as is indicated by the negative r value.

Table 4 shows the data for correlation of tone and tremor frequency in the control series of normals. Six of the seven parameters of Parkinsonian tremor had no counterpart in the normal. Therefore there is obviously no correlation with these parameters. However, the r value for the correlation of tone and tremor-frequency in the normal subject is a positive one. In other words, as tone in the normal muscle increases, frequency of the tremor increases. This is in contrast to what obtains in Parkinsonism. In the latter, as tone increases, tremor-frequency decreases. However, it is important to note that the r value in the Parkinsonian patient ($r = -.45$) is highly significant ($p = 0.01$),

whereas in the normal the r value of +.29 is above the 0.05 level of confidence and therefore lacks significance. Thus the correlation between tone and tremor frequency in Parkinsonism is a much stronger one, albeit reciprocal, than this correlation in the normal.

CORRELATION OF TONE AND TREMOR BY SUBJECTIVE MEANS

The subjective measurement of tone and tremor in Parkinsonism has been correlated by product moment correlation coefficients utilizing the data contained in Table 1. The r value for the correlation of tone and tremor in the right upper extremity is +.45 and in the left upper extremity +.30. Again a direct correlation between tone and tremor is demonstrated using subjective means. All correlations are depicted graphically in Figure 1.

DISCUSSION

As we have shown, there is a direct correlation between hypertonus and tremor abnormalities in Parkinsonism. There were five Parkinsonian patients who showed no tremor of the abnormal variety. In these patients, tone was likewise normal. There were eight patients who had normal tone and abnormal tremor. In the remaining 12, abnormalities of both tone and tremor were found. At no time was tone increased without associated abnormalities of tremor. However, there were eight patients with abnormalities of tremor who did not have increased tone. Thus if tone is increased, tremor always has some abnormalities. When tone is normal, tremor may or may not be normal. One might question, therefore, whether tone and tremor are due to a disturbance of the same fundamental neural mechanism.

The lower tremor frequencies in the Parkinsonian group are associated with hypertonus, whereas the higher tremor frequencies are associated with normal tone. One might postulate that the presence of hypertonus prevents the emergence of tremor of high frequency but permits the display of those of lower frequency.

We are unable to resolve with finality the question of whether tremor and rigidity in Parkinsonism are the same or different basic phenomena. However, we have shown that tone and tremor exert an effect on each other. Although it is difficult to state cause and effect, it appears that tone exerts an influence on tremor, with hypertonic states modifying the tremor parameters.

The definition of tremor as used herein is much expanded over that used by Jackson. He spoke of visible tremor and described only changes in amplitude and frequency as seen by the naked eye, as being changes in "tremor." However, with our improved method of measuring tremor, using the broader, more complete definition employing five parameters in addition to ampliture and frequency, we have shown that abnormal tremor in a qualitative sense occurs directly with increased tone when measured electronically. This direct relationship also obtains when tone and tremor are subjectively evaluated. These observations are in contrast to Jackson's statement of the reciprocal relationship between tone and tremor.

SUMMARY

Tone and tremor have been correlated in a series of normals, and in a series of Parkinsonian patients.

It has been shown that in the normal person, tone in an extremity and tremor frequency in that extremity tend to be correlated in a direct relationship. In Parkinsonism this relationship is in reverse.

In Parkinsonism, abnormalities of tremor may or may not be associated with hypertonus.

Hypertonus, however, is always associated with abnormalities of tremor of the Parkinsonian type.

Thus, in a qualitative sense, tremor and

tone abnormalities in Parkinsonism vary directly, both when measurement is objective and when it is subjective. These findings conflict with Hughlings Jackson's observations.

It would appear from this study that the phenomena of tone and tremor in Parkinsonism are separable, but when present in the same patient, there is mutual interaction and modification in a direct qualitative relationship.

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THE TREATMENT OF SCHIZOPHRENIA AND PSYCHOANALYTIC THEORY[1]

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The interaction between theory and clinical practice is a special version of the problems of the relation of thought and action. The correlation between the psychonalytic theory of schizophrenia and its treatment shows the customary phenomena related to learning; sometimes action is ahead of explicit formulation presumably because preconscious cognition of the task was more accurate than conscious conceptualization; at other times concept formation helps toward more successful intervention in reality.

A brief historical review of the relationship between theoretical and therapeutic advances in the understanding and treatment of schizophrenia will first be presented. Second, an appraisal of the current status of the problem will be made. Last, the writer will present and discuss a number of ideas with regard to an ego psychological psychoanalytic concept of the treatment of this disorder.

Freud's topographical model was predicated upon the fact that discontinuous behavioral phenomena could be seen as part of a continuum if one inferred that some links were, or had become unconscious. It followed then that psychoanalytic theory had to concern itself with intuitive hunches about the nature of the unconscious data, with the processes by which they became and/or remained unconscious, and with the processes of making them conscious. This basic theoretical framework applied as much to the treatment of schizophrenia as it did to that of the neuroses.

The first hypotheses formulated were that intolerable libidinous desires were repressed, that certain energy exchanges were involved in this process, and that interpretation of the content of the repressed drives was the road to cure. In that sense Freud's early topological model logically demanded a therapy predicated on the libido theory, namely, a therapy of content interpretation. It should be mentioned in passing that there are difficulties in deciding just when Freud treated schizophrenics and when neurotics, since it seems to us now that some of his brilliantly illuminating early cases of neurosis often would be considered schizophrenic today. There is little reason to hesitate in saying that in any case, content interpretation was the core of the treatment of schizophrenia.

For a brief time it appeared that Freud was the captive of his own semantics when he concluded that schizophrenics were suffering from a narcissistic neurosis[3] and

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[3] Hartmann has been particularly helpful in clarifying the relationship of the concept of narcissism to schizophrenia (14). It has been clear to many of us that schizophrenia often did not present well-developed narcissism in the sense of extreme self-love with its consequent lack of available affective feeling for others. Similarly, it had become clear that some character disorders often showed more self-absorption and self-love than schizophrenics. Hartmann specified that in schizophrenics it is not necessarily the self that is excessively invested, but rather some specific ego function. For example, thinking may be so narcissistically invested that words lose their propositional value and become objects *per se*, and are used as though they were objects, and often, different objects at different times. Thus, word magic, word play, and neologisms play a significant role in schizophrenia. Thinking and language have lost their adaptive function and attain a private and subjective function of their own.

It is important to emphasize this to make clear that schizophrenia cannot be diagnosed only by dynamic and economic characteristics of object relations. Some people who are schizophrenic give evidence of having reached oedipal levels of object relations with considerable cathexis of various figures; some non-schizophrenics often have not achieved so much.

ipso facto could not have enough libido available for transference, that object relationship so vital to successful psychoanalytic therapy.

Polemically, much has been made of this step in the evolution of his theory, but unjustifiably so. The neatness of the theoretical formulation was only a brief deterrent to Freud's understanding that narcissism must be seen as relative even in schizophrenia. By 1904, in a footnote in the "Three Essays," he had already revised his earlier view and considered schizophrenia amenable to psychotherapy (12).

Freud's great contribution to the understanding of psychoses was the Schreber case, which he published in 1911. Still, the emphasis was on understanding the content and the libidinal aspects of the illness. Only very recently have some more of the building stones of Schreber's delusions and hallucinations been uncovered by the fascinating work of Niederland (18). There are still aspects of psychotic development about which we are very much in the dark. In the case at point we would certainly like to know the dynamics by which some of the experiences at the hand of his father translated themselves into psychotic manifestations.[4]

It would be a mistake to believe that there was a simple lineal development in Freud's thinking, and that one day the quanta jumped from the topographical to the structural model. As we now know, he had in mind many of the concepts concerning ego psychology as early as 1895 in the long-unpublished "Project for a Scientific Psychology" (11). Even without the "Project" it is clear that Freud described defense mechanisms such as projections as early as 1894 in his papers on "Anxiety and the Defense Neuropsychoses" (9, 10). In "Totem and Taboo" (13) he considered projection a part of normal everyday perception. In that paper one can see in essence a discussion of the perceptual functions of the ego much as it has become again the basis for current perceptual theories of personality.

It was many years before the heavier accent on ego psychology, as indicated in Freud's works from 1924 on, Anna Freud's in 1936 (8), and Hartmann's monograph, "Ego Psychology and the Problems of Adaptation," in 1939, made itself felt in the treatment of schizophrenia. Sullivan's and Fromm-Reichmann's contributions to the treatment of schizophrenia in the early 1940s, though outside classical psychoanalytic theory, undoubtedly served as a powerful, albeit indirect stimulus even upon orthodox psychoanalytic theory in the treatment of schizophrenia. Indirectly, their contributions made Federn's work better known, possibly as a somewhat more orthodoxly acceptable counterpart (6). Today, however, one still cannot say that the principles of ego psychology are being systemically applied to the treatment of schizophrenia.

Interestingly enough, the treatment of schizophrenia which caused most excitement and comment in this last decade, John Rosen's 'direct psychotherapy' of schizophrenia, was entirely devoid of ego-psychological sophistication. It addressed itself to content interpretation of a rather unsystematic nature (19). As Eissler has remarked, his approach is probably useful as a non-specific support in the acute phases.

The most illustrative record of the state of schizophrenia therapy over the last ten years is probably the book edited by Brody and Redlich in 1952 (5). In this volume a number of workers in this field discuss their particular and varied views. In reviewing this collection of papers at the time of its publication I found as a striking aspect the

[4] Some modification of Fischer's work (7) on perceptual aspects of the dream-work might be usefully applied to the study of the formation of delusion and hallucination in psychoses by exposing subjects tachistoscopically to perceptual stimuli before or during the induction of an experimental psychosis with chemicals like LSD, or by perceptual isolation.

lack of any systematic approach to the treatment of schizophrenia. Each contributor had his particular approach to which he adhered for most, if not all, of his patients. Eissler was relatively most specific in pointing out that the acute phase of schizophrenia may well respond to any sympathetic relationship but that the 'clinically mute' chronic character disorder which is part of the psychosis needs prolonged, detailed, and skilled individual analysis. In this latter point of view, he and Fromm-Reichmann were in essential agreement.

It seems that up to the present, each therapist chooses for himself either one particular ego function as *the* important aspect of the personality with which to work, or elects one particular approach to the improvement of *all* ego functions. The vicissitudes of the results in our various current treatments lead me to believe that one cannot elect any one particular ego function on which to concentrate therapeutic change that will suit all cases; and further, individual approaches must depend on the specific patterns of disturbance and must be worked out to suit the individual case at hand. In other words, there is no one and all-inclusive method of approach.

The most etiologic and systematic therapeutic approach has been made by Sechehaye (21). She believes that the treatment of the disorder has to concern itself with a supplementary acquisition of ego functions which were either never acquired or massively lost by regression. The patient must learn from the therapist what he never learned from the parental figures, or did not learn well enough. Sechehaye indicates that the level and nature of the therapeutic intervention should be predicated on the level and kind of regression or lack of progression involved; preverbal or verbal, involving different functions and even different sense-modalities. In that sense, one might say that she has devised a 'phase-specific' treatment of schizophrenia that is completely geared to suit the individual patient. Sechehaye's work highlights the important role that ego psychology and object relations play in the current theory and treatment of schizophrenia.

I have myself attempted to apply Spitz' findings (22, 23) concerning the earliest severe disturbances of object relationships to the etiology of schizophrenia, particularly in the so-called "nuclear" type, and also in cases of "simple" schizophrenia (1). Certain somatic abnormalities appear to be best understood as the physiologic result of a severe disturbance of object relations in infancy.

Mahler has described a later object disturbance as responsible for *symbiotic* psychosis (16). Predicated on this concept is a treatment approach that emphasizes establishment of ego boundaries and the recognition of the self as a separate entity.

The propositions of Melanie Klein concerning earliest object relations are the basis of much schizophrenia therapy and are used in particular by Rosenfeld (20). Klein's ideas are untenable for many psychoanalysts because it seems difficult to accept, and impossible to verify, that all object relations should be predicated so predominantly upon extremely early perceptual processes. Nevertheless, many of the phenomena she speaks of, for instance "the incorporation of the bad breast" or "the paranoid position" often seem to have explanatory value in therapy. My own feeling is that Klein recognized certain events correctly, but dated them developmentally too early and over-stated and over-generalized their importance.

Although the propositions concerning disturbances in object relations in schizophrenia are of utmost importance, they have left some misconceptions in their wake, and have often not been clearly enough formulated in relation to conceptions of treatment. Obviously object relations are the matrix for all psychological behavior. It is only via one's relations to animate and inanimate things that there can be per-

ceptual learning, drive direction, impulse control and other functioning. Because schizophrenic patients have shown such obvious disturbances in relating to people, the idea has been held that any form of good relationship to an individual, therapist, or group, would be of major therapeutic value.

The fact is that the disturbances in object relationships are as manifold as the forms of relations to objects; perceptual, logical and libidinous relationships are merely a few of those that must be kept constantly in mind. In terms of ego function, the treatment of schizophrenic disturbances in object relations has to be tailor-made to fit each individual case.

It is such considerations as these that bring me to the statement of my personal credo. Any sound therapeutic intervention must be based on a sound theory of the multifarious nature of schizophrenia. This dictum holds true even in the eventuality that some forms of this disorder may prove to be, to greater or lesser degree, of a primarily organic nature. In the case of organic pathology we are simply talking about the problems of learning or relearning certain ego functions never acquired, or lost, due to afflictions of the organic substratum.

The writer's suggestion, stated previously (1, 2), has been a multiple-factor psychosomatic theory of schizophrenia; that the syndrome of schizophrenia may be the result of any number of psychogenic and somatic factors which share as a final common path the severe affliction of the ego and its functions. I have suggested that we borrow D. Wechler's model of intelligence as a model of ego functioning. We would have then a global quality which could be characterized, studied, and even measured to some reasonable degree by a study of its functions, its adaptations, drive controls, frustration tolerance, perceptions and so on.

One of the main facts to remember is that different people suffering from what we subsume under schizophrenia are affected not only for different etiological reasons but also in different ways; plainly, the pattern of ego disturbance differs from patient to patient. It may be possible to speak of features which are shared to a certain point by many or most schizophrenics, but we cannot go beyond that without subdivision. Classification might include, for example, the sociopathic, the infantile, the simple schizophrenic, etc. but, whatever system of classification seems the most workable, one must never lose sight of the very individual features of the case. A rational treatment of schizophrenia must be based on a conceptualization of the ego functions which are especially disturbed in each patient. Once the pattern of disturbance has been established it is time to plan the specific strategy and tactics of improving the pattern of ego function.

In cases of "infantilism" that are diagnosed as schizophrenic because of the extreme lack of ego functioning, the simple, need-satisfying type of behavior has to be modified by actually teaching frustration tolerance, anxiety tolerance, and all the complexities of detour behavior that stand between drive-demand and drive-gratification in our culture. Such patients often had parental figures who were inconsistent and never provided sufficient structure in the upbringing of the child. Treatment in these cases means the building of controlling apparatus, the teaching of a hierarchical set of behavioral patterns. "Teaching" and "learning" that postponement of gratification may bring greater satisfaction than immediate gratification, and that immediate drive fulfillment may often bring almost immediate punishment, may be done in part by conditioning actual behavior in a therapeutic group or perhaps in individual therapy by using the patient's adult intelligence for learning by abstraction and insight. What can be seen in this approach holds true for many schizophrenics; ther-

apy often does not deal with *reversing regression* but with providing learning experiences that had never been acquired because of a *lack of progression*. For this reason we must think more often in terms of habilitation rather than rehabilitation, of enabling rather than reenabling by whatever variety of means. The process of deneutralization and defusion of drives that Hartmann speaks of in his discussion of the vicissitudes of drive energy is often matched by a lack of attainment of any neutralization or fusion of drives.

Compare now the infantile type of patient and his undifferentiated nature, to the successful young professional who is also diagnosed as schizophrenic by virtue of his paranoid delusions and hallucinations. The latter individual has a highly differentiated personality but one particular aspect of his object relations is severely disturbed. The image of an enema-wielding mother is reinforced by a teasingly controlling father, and together, speaking schematically, is responsible for an apperceptive distortion of *all authority* figures. He sees them as potentially dangerous, ascribing to them not only the characteristics of the internalized parental images but also his own hostility for the parents—a mixed form of projection. Under a particularly strong impact of anxiety, fear, and hostility, his self-boundaries become ill-defined and he fails to differentiate thought process from perception. Here, any psychotherapy more than merely symptomatic must consist of analyzing and reducing to their common denominator his apperceptive distortions, tracing the historical genetic components that make them up, and working through his insights in the transference situation and in other settings. He must learn to recognize "signals" of anxiety and hostility that initiate a loss of ego boundaries and perhaps accompanying feelings of depersonalization. Once recognized, he has to learn to analyze the situation for himself, that is, to make himself aware of the threatening components and thus prevent ensuing distortion. After much repetition we can hope that ultimately he may indeed restructure his earlier experience of the internalized images to a point where he will automatically perceive authority figures relatively undistorted. The stability of such and any psychoanalytic cure is really a question of the stability of recently acquired learning and relearning as compared to the tenacity of earlier learned material[5].

The two types of patients briefly discussed have disturbances of ego functions. In the first, it is a matter of acquiring control of drives and impulses as the very fundaments of ego structure; in the second, a matter of relearning specific apperceptive sets. Compare this now to a schizophrenic in which a thinking disorder is the outstanding symptom. Here too there is a disturbance in object relationships, but now it starts on the propositional level concerning objects in the broadest sense and involving their roles and meanings. If this disturbance in thinking is due to a lack of consistent learning in childhood, perhaps because of inadequate contact with adult figures, perhaps because of linguistic difficulties, perhaps because of such poor object relations that verbalization never quite developed, no amount of "good" therapeutic relationship to individual or group will have real value. The only hope for this "backward" patient is a systematic retraining similar to what Sechehaye has done with very regressed or un-progressed patients. If this thought disorder exists to a lesser degree, long-drawn-out, meticulous, and repeated reality testing, learning of concept-formation, and establishing of ego-boundaries in individual modified psychoanalysis might be of value.

The simple schizophrenic results from a lack of structural development in childhood

[5] American academic psychology is in the habit of subsuming *all* experiential data under the heading of "learning," a custom as useful systematically as it is confusing to those not acquainted with it.

because of disturbed object relations. I believe that a lack of afferent impulses in infancy and childhood may be seen as responsible for the lack of somatic and psychic delelopment of these patients. Spitz speaks of certain children as suffering from a psychic deficiency disease. His propositions are quite consistent with Magoun's findings (17) that there is an afferent apparatus which responds to the total amount of sensory input; that insufficient stimuli bring about a lack of physiological development and organization in addition to a lack of psychic structure. This could account for the lack of drive, of differentiation, of even delusional or hallucinatory adaptation that is found in Schizophrenia Simplex. In its extreme, this constitutes a practical limitation to reversibility of any extent.

Between and intermingled with such extremes as these lie the multitude of individual patterns and disturbed ego functions, all of which require specific care. Hartmann has provided a most comprehensive theoretical contribution to the metapsychology of schizophrenia (14). He examines the nature of object relations as well as defensive functions, but pays particular attention to the vicissitudes and economics of drives and drive energy. He speaks not only of quantities and their distribution, but also of a continuum from fully instinctual to fully neutralized energy.

Some of Hartmann's theoretical points are particularly useful. He points out that not all ego functions are disturbed in any given individual, and especially emphasizes that certain functions remain intact. Most of the autonomous functions such as intelligence, memory, and gross perception which classically differentiate schizophrenia from organic psychosis, remain. He follows Katan (15) in speaking of a *residual personality* in schizophrenics, referring to the *intact residue.*

This point leads me to emphasize that the assessment of patterns of ego functions should not only include the areas of disturbances which we as pathologists are so likely to focus on. It should also clearly state the *assets* of remaining good functions. Therapy will then have to be directed not only towards improving impaired or never acquired functions but also specifically to make use of the still *intact functions.*

Unless one follows some such scheme of appraising ego function as I have described (2), I think that psychological tests should be used as a systematic aid in arriving at a "profile" of ego functioning. We found a relatively rough rating of ego function, aided by psychological testing, useful in rehabilitating schizophrenics (3, 4).

It is in working with the intact residue, *e.g.*, high intelligence, an almost autonomous ability to work, a good ability to use anaclitic relationships, an obsessive capacity to function within a rigid setting, that one sees most clearly the possible paths towards rehabilitation. In the rehabilitation program at Altro (3) we were often successfully more ambitious than just stated. We had thought of the workshop as a place for learning or relearning object relations in a controlled environment. The efforts of the social worker and the psychiatrist were often "therapeutic" in trying to resolve apperceptive distortions, build frustration tolerance, etc. But for severely regressed, "nuclear," "burned out" schizophrenics it was indeed often a matter of working with and making the most of the remaining defenses and other ego functions.

In conclusion, it should be stated that not all therapy understood in terms of ego psychology need be psychotherapy. Organic treatment may play a very useful role in the case of patients with great difficulty in sustaining any tension and with a good many affective components. It appears that insulin or the tranquilizing drugs can sometimes decrease the drive-push to a point where the ego, with or without psychotherapy, can perform its synthetic function better; in cases of acutely precipitated psychoses the reversal of symptoms

may actually lead to a fairly stable new equilibrium; in other cases some further decrease in synthetic ego function may be halted unless or until psychotherapy provides for further restructurization.

Similarly, I believe that the various sleep treatments are forms of suspending most ego functions, thereby indirectly permitting a spontaneous internal realignment of forces to a better synthesis. The absence of external stimuli is probably equalled in significance by the relative suspension of internalized imagery.

ECT is unfortunately still a blind procedure. If all goes well it has a drive-repressive *or* "control" repressive effect which is probably coincident with Lashley's concept of mass action; enough quantitative tissue is affected for the time being to produce qualitative behavioral changes. Secondarily this effect may permit better adaptive and synthetic functioning of the ego again. It is part of the uncertainty of ECT that one cannot predict whether drive-repressive or control-repressive effects will ensue; thus often the yield is the undesirable result of the one when what is needed is the other. This is particularly true of patients who become more overactive, more uncontrolled, and less integrated or more paranoid then they were before. The same, much more dramatically, has often held for lobotomies.

In an ego psychological sense, I would have considered thalamotomy or hypothalamic electrotherapy etiological forms of treatment in extremes of drive disturbances which are refractory to every other approach. It is unfortunate for both theoretical and practical reasons that these methods have not developed successfully.

SUMMARY

The theoretical background of psychoanalytic treatment of schizophrenia was originally oriented along the lines of the libido theory and content interpretation.

Although ego psychology has played an increasing role in psychoanalysis, it has not played a major role in the treatment of schizophrenia until very recently. Even today it is hardly taken into account systematically. Many therapists seem to choose for themselves either one particular function to work with in all patients, or to choose one particular approach to affect any disturbance.

Rational treatment of schizophrenia must be predicated upon a clearly conceptualized picture of the disorder, as follows.

The schizophrenic syndrome is characterized by a global disturbance of ego functions of a severe degree and of different etiology.

Different schizophrenics have differing patterns of disturbance of ego functions which can be well stated in terms of psychoanalytic metapsychology, in quantitative and qualitative patterns or profiles.

The treatment of each individual schizophrenic patient must be designed to improve his specific ego functions; those never acquired by failure of progression or those lost by regression. The intact personality residue must be utilized to the fullest in this process.

Improvement in ego functioning can come about by different therapeutic means, at least initially or for moderate goals, although ideally some form of psychotherapy is always likely to be needed to improve or stabilize the therapeutic attainments of other methods of treatment.

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because of disturbed object relations. I believe that a lack of afferent impulses in infancy and childhood may be seen as responsible for the lack of somatic and psychic delelopment of these patients. Spitz speaks of certain children as suffering from a psychic deficiency disease. His propositions are quite consistent with Magoun's findings (17) that there is an afferent apparatus which responds to the total amount of sensory input; that insufficient stimuli bring about a lack of physiological development and organization in addition to a lack of psychic structure. This could account for the lack of drive, of differentiation, of even delusional or hallucinatory adaptation that is found in Schizophrenia Simplex. In its extreme, this constitutes a practical limitation to reversibility of any extent.

Between and intermingled with such extremes as these lie the multitude of individual patterns and disturbed ego functions, all of which require specific care. Hartmann has provided a most comprehensive theoretical contribution to the metapsychology of schizophrenia (14). He examines the nature of object relations as well as defensive functions, but pays particular attention to the vicissitudes and economics of drives and drive energy. He speaks not only of quantities and their distribution, but also of a continuum from fully instinctual to fully neutralized energy.

Some of Hartmann's theoretical points are particularly useful. He points out that not all ego functions are disturbed in any given individual, and especially emphasizes that certain functions remain intact. Most of the autonomous functions such as intelligence, memory, and gross perception which classically differentiate schizophrenia from organic psychosis, remain. He follows Katan (15) in speaking of a *residual personality* in schizophrenics, referring to the *intact residue*.

This point leads me to emphasize that the assessment of patterns of ego functions should not only include the areas of disturbances which we as pathologists are so likely to focus on. It should also clearly state the *assets* of remaining good functions. Therapy will then have to be directed not only towards improving impaired or never acquired functions but also specifically to make use of the still *intact functions*.

Unless one follows some such scheme of appraising ego function as I have described (2), I think that psychological tests should be used as a systematic aid in arriving at a "profile" of ego functioning. We found a relatively rough rating of ego function, aided by psychological testing, useful in rehabilitating schizophrenics (3, 4).

It is in working with the intact residue, *e.g.*, high intelligence, an almost autonomous ability to work, a good ability to use anaclitic relationships, an obsessive capacity to function within a rigid setting, that one sees most clearly the possible paths towards rehabilitation. In the rehabilitation program at Altro (3) we were often successfully more ambitious than just stated. We had thought of the workshop as a place for learning or relearning object relations in a controlled environment. The efforts of the social worker and the psychiatrist were often "therapeutic" in trying to resolve apperceptive distortions, build frustration tolerance, etc. But for severely regressed, "nuclear," "burned out" schizophrenics it was indeed often a matter of working with and making the most of the remaining defenses and other ego functions.

In conclusion, it should be stated that not all therapy understood in terms of ego psychology need be psychotherapy. Organic treatment may play a very useful role in the case of patients with great difficulty in sustaining any tension and with a good many affective components. It appears that insulin or the tranquilizing drugs can sometimes decrease the drive-push to a point where the ego, with or without psychotherapy, can perform its synthetic function better; in cases of acutely precipitated psychoses the reversal of symptoms

may actually lead to a fairly stable new equilibrium; in other cases some further decrease in synthetic ego function may be halted unless or until psychotherapy provides for further restructurization.

Similarly, I believe that the various sleep treatments are forms of suspending most ego functions, thereby indirectly permitting a spontaneous internal realignment of forces to a better synthesis. The absence of external stimuli is probably equalled in significance by the relative suspension of internalized imagery.

ECT is unfortunately still a blind procedure. If all goes well it has a drive-repressive *or* "control" repressive effect which is probably coincident with Lashley's concept of mass action; enough quantitative tissue is affected for the time being to produce qualitative behavioral changes. Secondarily this effect may permit better adaptive and synthetic functioning of the ego again. It is part of the uncertainty of ECT that one cannot predict whether drive-repressive or control-repressive effects will ensue; thus often the yield is the undesirable result of the one when what is needed is the other. This is particularly true of patients who become more overactive, more uncontrolled, and less integrated or more paranoid then they were before. The same, much more dramatically, has often held for lobotomies.

In an ego psychological sense, I would have considered thalamotomy or hypothalamic electrotherapy etiological forms of treatment in extremes of drive disturbances which are refractory to every other approach. It is unfortunate for both theoretical and practical reasons that these methods have not developed successfully.

SUMMARY

The theoretical background of psychoanalytic treatment of schizophrenia was originally oriented along the lines of the libido theory and content interpretation.

Although ego psychology has played an increasing role in psychoanalysis, it has not played a major role in the treatment of schizophrenia until very recently. Even today it is hardly taken into account systematically. Many therapists seem to choose for themselves either one particular function to work with in all patients, or to choose one particular approach to affect any disturbance.

Rational treatment of schizophrenia must be predicated upon a clearly conceptualized picture of the disorder, as follows.

The schizophrenic syndrome is characterized by a global disturbance of ego functions of a severe degree and of different etiology.

Different schizophrenics have differing patterns of disturbance of ego functions which can be well stated in terms of psychoanalytic metapsychology, in quantitative and qualitative patterns or profiles.

The treatment of each individual schizophrenic patient must be designed to improve his specific ego functions; those never acquired by failure of progression or those lost by regression. The intact personality residue must be utilized to the fullest in this process.

Improvement in ego functioning can come about by different therapeutic means, at least initially or for moderate goals, although ideally some form of psychotherapy is always likely to be needed to improve or stabilize the therapeutic attainments of other methods of treatment.

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DISRUPTION OF ADULT EGO IDENTITY AS RELATED TO CHILDHOOD LOSS OF A MOTHER THROUGH HOSPITALIZATION FOR PSYCHOSIS[1]

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Erik Erikson (5) speaks of the common life crises shared by a group of young, severely disturbed, borderline patients aged eighteen to twenty-four who suffered from acute identity diffusion. The somewhat later adult years, after twenty-five, also can be associated with identity crises, and it is the purpose of this paper to describe such acute identity disruptions in adult patients. They faced a common life crisis, though different from the one Erikson found in his younger group of patients. Our patients all had married and become parents, and they had had permanently hospitalized psychotic mothers. Our investigation sought to find the discernible effects of the psychotic mother on the individual who undertook the role of motherhood with the background of this experience in her own childhood.

Cases fitting this description are quite rare because we are referring to permanent, not transient, hospitalization of the mother during the patient's childhood. We stipulated permanent hospitalization prior to age 16 so that this group of patients (where loss of the mother had occurred through hospitalization for psychosis) would meet the same general criteria as another experimental group from the same hospital where loss of the mother had occurred through death prior to the patient's sixteenth birthday (12). Though these cases of permanent loss through psychosis are rare, their great theoretical interest persuaded us to conduct the intensive search needed to uncover even a few of them for whom the life history data would be adequate to permit a study of two-generation dynamics. They are of special importance from the point of view of ego development because of the extreme childhood trauma followed by relatively inconspicuous early pathology but leading much later, after parenthood, to a psychotic break often resembling that of the mother. Admission records of women who entered the hospital during a nine-month sampling period in each of four years, 1954 through 1957, were screened to find all cases in which the relevant data were clear and conformed to the pattern 1) that the mother was reported as permanently hospitalized before the patient's sixteenth birthday and 2) that the patient had not entered any mental hospital before marriage and parenthood. We were able to locate fourteen such patients. These patients were investigated, some more intensively than others. It should be noted that we do not have a general population sample of individuals whose parents became permanently psychotic when their children were young; thus, all those studied were necessarily patients and the hypothesis

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tested has to do only with the precipitating event and its deeper ramifications. In this study we have no evidence bearing on the total frequency of psychoses among women who lost mothers in childhood through the mother's permanent hospitalization.

The pool of 757 women, married and with children on first admission from which these fourteen patients emerged, will be described in a statistical summary now in preparation (13). This statistical summary reports on parental losses in childhood due to death, and is designed as a test of the anniversary hypothesis both on a statistical and clinical basis. Some of the problems of control in this kind of study, missing from the present paper, are there handled by appropriate statistical tests. It should be noted that *all* patients who met the criteria were studied. Thus, though the numbers are small, there was no bias in selection based upon information bearing on our hypothesis.

These fourteen unselected cases of women whose mothers had been permanently hospitalized for psychosis proved of great significance because of the high percentage that conformed to the anniversary hypothesis. This hypothesis had been found previously to explain some of the late appearing cases of schizophrenia where the patient, during childhood, had experienced the loss of mother through death (10, 12). Among these fourteen cases, nine conformed to the anniversary hypothesis, in the sense that each entered the hospital as a patient when she had a first or second child who was within a year of the age she had been at the time of her own mother's permanent hospitalization. Since ten of the fourteen cases were treated psychotherapeutically, we have considerable dynamic material to supplement the fact of age coincidences.[3] We shall return to a consideration of these age coincidences after reporting one of the cases in greater detail to illustrate the kind of material with which we have dealt.

[3] While we believe that the dynamic relationships uncovered have relevance for the direction of therapy, we are postponing consideration of therapeutic procedures and outcome for a separate report.

CASE OF MARIA F.

Maria F. was a 32-year old, white, Catholic housewife. She lived at home with her husband and two children, a son aged seven and a daughter, aged four years and one month. Her illness started suddenly with headaches for one week prior to the acute break, and she associated headaches with insanity. She awakened one night trembling, very depressed, and suicidal. She said she was the Virgin Mary, had a mission to fulfill, and that she had had intercourse with God. She wet her bed and called herself "naughty little girl." She expressed fears of killing her daughter. She heard voices saying words like "kill" and "child." The following day she went to a psychiatrist. On her return home she said that the doctor had made her remember her childhood, and then she screamed, "I killed my mother . . . " The patient then told her husband that her father had once said to her, "You will be the death of your mother . . . " Next she told her sister as they looked at some cats on a near-by roof, "I must have been like a cat as a child, sneaking around. I peeked into a keyhole when I wasn't supposed to—lots of blood, blood all over." Then she screamed and cried. She recalled repeatedly an incident that occurred at Christmastime the week before her mother was taken to the hospital when the mother had suddenly hurled two dolls belonging to her and to her sister into the fire. The patient said to her sister, "You were so unhappy and so was I. It could have been a baby." She was hospitalized immediately.

We did not see her in treatment until six months later. We interviewed the husband, brother, and sister and searched for particular environmental strains in the period preceding onset of this acute symptomatology. No critical incidents of an upsetting nature were found.

The patient was the second of four chil-

dren, with an older brother, a younger brother, and a sister as the youngest child in the family. The foreign-born father had been a rancher. The patient's brother described the father thus, "As a small child I was frightened of him. He was furious when we would make a lot of noise. As I was older, I became fond of him, he was interested in us and had no life of his own; he lived for us." Her sister spoke of the patient's relation to her father, "It was all right, but she didn't get a lot of affection. She thought he didn't like her; maybe *shouldn't* like her, she said as she was getting sick."

The mother, also foreign-born, came to this country in her teens. From the state hospital record we learned that she was hospitalized at age 35, when our patient was seven years old. The acute onset had begun a week before entry, which would have been shortly after Christmas. She became noisy, excited, violent, destructive, and threatened suicide. The history was uninformative except for the fact that for the preceding five years she had had "hysterical" attacks lasting three to four days with her menstrual periods. When the patient was 13, she and the other children were taken to see the mother, who remembered the first two children but not the younger two. The patient thought something must have happened to the mother after her birth, since she was the second child. She commented that she resembled her mother in appearance. "My father always told me how much I looked like my mother. We had a picture of her. I do look like her except she was dark. Other people said that too." The rest of the family thought that something had happened to the mother so that she had never been as well after the birth of the youngest child, who was born a month after the patient was four.

After the mother's hospitalization, the children were cared for by two aunts. They watched for mental symptoms in the patient, saying that she was like her mother, that she had temper tantrums, etc. The sister described the patient's childhood personality, "she was outspoken, quick to let people know what she didn't like, obstinate. She read a lot. All of us were shy."

The patient graduated with average grades from the university, and then married, instead of teaching school as she had intended. The marriage was described as a satisfactory one by both the patient and her husband. She was frigid at first; intercourse had been painful. It now occurred about once a week and the patient did not look forward to it though she had an orgasm. Her husband, an excellent salesman, held a responsible position. As a boy he had been shy, introverted, preferring tinkering with a radio to playing with other boys, and never participated in sports or competitive games. He was quite dependent on his wife, easily given to feelings of depression. In general, the patient had done everything around the house and yard, managed and dominated her husband.

The children included Richard, who was seven years old at the onset of the patient's illness, and Priscilla, who was four years and one month. Richard was an asthmatic child, quite close to the patient. Maria F. herself was small, pretty, thin. Priscilla was described by the patient's sister as "the spitting image of her mother.... Before she took sick, Priscilla was her mother's joy but drove her to distraction. She feels Priscilla is very much like she was as a child. She is sensitive, small, stubborn, given to moods, needs a lot of affection, but is so annoying you snap at her when you shouldn't." The patient had much less trouble with her son though she was worried about his asthma.

A number of our cases have some common features that differ from the classical pictures of schizophrenia, though they are almost without exception diagnosed as paranoid schizophrenia at the hospital. Maria's emotional reactions illustrate some of these common features. She was in contact with

the therapist and established a dependent relationship almost immediately. At times she could stand aside and look at her delusions. She was able sometimes to express feelings with the appropriate words. Within the first few hours there were tears. There was responsive laughter with no autistic laughter at any time. She was extremely vulnerable to separations from the therapist soon after therapy began. She also showed intense jealousy of other patients who were being treated by the same therapist. This behavior, on a transference level, was in a sibling rivalry pattern. Her responses to these situations included death wishes and fears of imminent death.

Let us concentrate our attention on the clues to ego identity and diffusion phenomena as shown by this case.

Clearly definable in the clinical and therapeutic material are two early identifications, neither capable of becoming dominant. The first identification is with the psychotic mother as the patient experienced her in childhood. The second is with herself as child vis-a-vis that mother, reinstated now by the presence of her daughter. Most memories and much of the re-living phenomena show the indistinct boundaries that now exist between these two areas of the ego.

A few illustrations will be given of the patient's preoccupation with herself as psychotic mother, the first of these two identifications.

In regard to the timing of her illness, she said, "I think it's because my mother was taken to the hospital when she was 32 and I was going to be 32." The patient was hospitalized two weeks after her 32nd birthday. Her first preoccupation with dating her mother's illness followed the birth of Priscilla, that is, when she became the mother of a daughter. She had figured out the mother's age from knowing her age at marriage and the spacing of the children. (Actually the mother was 35 years old, but there is no evidence that the patient knew it.) Even before Priscilla's birth, she had begun to fear mental illness. "A mental illness has been a conscious fear ever since I got married." Here we see fear of the emerging identification with the psychotic mother at the time her role changed to that of a wife. When the role later included that of being a mother, the identification with the person who had been a wife and mother during the patient's childhood years gained momentum. The mother's teeth, which had been extracted shortly before the acute illness, had always been associated in the patient's mind with her mother's breakdown. Shortly after marriage, the patient's teeth began to show more cavities, a process that accelerated to the point where, after the birth of her second child, extractions became increasingly necessary.

She identified with her mother in feeling that the mother had all the children she wanted after the birth of the patient, who was the second child and first daughter. There may have been some basis for this assumption since, the one time all the children visited their mother at the hospital, she recognized the elder two but not the last two. The patient explains, "It's so much the same today as it was when I was a child. I had an older brother, and there are a boy and a girl now . . ." "My mother had all the children she wanted after she had me. Just the way I felt with two children. After I had my daughter that was enough . . ." An additional incident of similarity involves her recall with horror of the mother's throwing the two dolls into the fire; the patient dreamed that two babies were thrown into a fire.

In this last incident we see the patient as child, she who had experienced and interacted with the sick parent. We now note the persistence in the present of her identification with the child she was many years ago. We recall that as her illness started she wet her bed and called herself a "naughty little girl," that she recoiled with terror as she remembered seeing blood through a key-

hole, a scene that probably referred to the birth of the younger siblings at home. Memories of masturbation experiences as well as sexual play with her brothers were reinstated in her psychotic productions.

This brings us to the meaning to the patient of her children, and their role in reviving conflicts over identification. With tears, in one of the early treatment hours, she said, "I named her Priscilla on purpose. I thought I wanted a little girl very badly. I wanted to name her Priscilla after my mother, for I'd be making up for something to my mother who had been left all alone. . . . I'd see that my little girl was very happy, and that would be making up to my mother."

The coincidence of age of the mother's actual hospitalization comes not with the age of Priscilla but with that of son Richard, aged seven. In most of our cases, the relationship is with the oldest child. Because the oldest child happened to be a boy, there is a displacement and a double identification of herself with Richard, who is the age she was, and of herself at four years and one month with Priscilla. Shortly after the patient was four, the mother had been quite upset following the birth of her youngest child. It was most likely this birth which the patient saw through the keyhole. One of the patient's symptoms in the early hours of treatment was the conviction she was pregnant, along with extreme anxiety about it.

There are many circumstances here to re-integrate an earlier emotional experience for the patient, such as the presence of a child named for the mother, an age patterning of children, and similar conditions that make for parent-child tensions. A strong motif is guilt. She says, "I caused my mother's illness," or in another statement, "I killed my mother." Death and disappearance by psychosis are equated. She comments, "What if the children think it's *their* fault that *I'm* in the hospital?" There is evidence that the patient had been alternately indulged and hated by her mother, just as we hear that Priscilla has been both the joy and the bane of the patient's existence. "I was my mother's first daughter. I was very important to her because I was. My daughter is important to me in the same way without my feeling like a real mother to her. I don't know quite what I mean." The patient went on to say that her aunt spoiled *her* first daughter very much, that it is done this way among her people. There is indirect evidence to support the patient's assertion of a special position; for instance, in her school history she was the teacher's pet in several grades. The negative part of her mother's ambivalence was expressed symbolically with destructive violence in her illness.

These two strong, shifting identifications, the first an identification with her own mother and the second an identification with her daughter, are highly conflictual. One reason for the pathological outcome of the conflict is the oedipal rivalry re-awakened by the presence of a rival daughter. Through her identification with her daughter, there are clues to the patient's own oedipal conflict. "Just before I got ill I had a dream of being raped by a horse. The horse reared up and hit at me with its hoofs. A great, big, shiny, reddish brown horse. Oh no, it didn't rape me. I was only afraid that it would." This is the dream of the oedipal child. In a later hour talking spontaneously of her feelings toward her children, she said, "Priscilla acts as if she *was* me and was furious with me for interfering with her plans—as if in a way she thought my husband was hers, not *mine*." . . . "I had such a scary idea once that my husband was going to rape my daughter." She said her father had rarely turned down anything she really asked for. In speaking subsequently of her mother she made a slip, "When mother was with us, my husband—I mean my father—was doing very well."

The desire to possess her father after her mother's death was defended against by a

withdrawal from active expressions of affection toward him and by some hints of a masculine identification. At the time of her first menstruation, she said she wanted to be a boy. Later she also feared she was homosexual: "I was afraid I was homosexual, or not quite female when I didn't enjoy intercourse.... I felt masculine. It wasn't very unconscious for a while. I thought I would love to be a boy, and I'd never have any children after I started menstruating. I was going to be a school teacher—they didn't get married or have children. They were less dependent."

After the intense rivalry with her mother, which appeared to result in the mother's permanent expulsion from the home, it is clear why she was unable to handle the rivalry of a daughter. She projected her own feelings upon this child, who would wish for her expulsion, and might be expected to achieve it. Would she deserve this fate at the hands of her daughter as punishment for what she had done to her mother?

The patient had been unable to work through this problem during latency and adolescence because of her own withdrawal, her father's personality, and the lack of a normal reconstruction of the family.

We have presented this case in some detail because it illustrates so clearly the persistence into adult life of confused and unintegrated identifications in a person who at the same time managed to achieve a sufficiently intact ego to graduate from college, to marry, to bear two children and raise them through their early years. But what identity had been achieved was too fragile to survive a crisis in which the circumstances surrounding the early trauma were repeated. Had these circumstances not occurred—for example, if she had not had a daughter—it is quite possible that a psychosis could have been avoided. It is of interest that this growth crisis was postponed until the early thirties, as distinguished from the crises in the early twenties reported by Erikson.

RELATED CASES

The other cases, in one way or another, all show circumstances surrounding childhood trauma repeated coincidently with the onset of psychosis. We may return here to the earlier statement that in nine of the total group of 14 cases where a mother was permanently hospitalized during the patient's childhood, the patient at onset had a first or second child who was within a year of the age she had been at childhood loss of her own mother. Clinical material gained both from relatives and from therapy with the patients bears out the fact that a major determinant in the identity crisis can be the presence of a child. Parents can and do respond to their children's developmental level with reactivation of their own unresolved childhood feelings and fantasies (2). These ages at loss of mother in the nine coincidence cases range from 22 months to 15 years. The patient whose mother was hospitalized when she was 22 months of age was hospitalized when her daughter was 22 months of age. A patient whose mother was first hospitalized with a postpartum when the patient was two years old, was hospitalized with a postpartum when her daughter was three; her mother's second and permanent hospitalization took place when the patient was six, and the patient entered the hospital for the second time when this same daughter was six. Of the nine cases, four patients were under six, one was seven, and four were between the ages of 12 and 16 at the time of the mother's hospitalization.

The median age of our patient group at hospitalization was in the early 30's. This had been the approximate age of hospitalization in the maternal generation though in the nine cases of coincidence with childhood age there is none within a year of the maternal age, suggesting that the exact age of the child at the time of the mother's hospitalization is the determining factor. Six of the nine patients were Protestant, three were Catholic. Their educational level ranged from eighth grade through college

graduation with the median at three years of high school.

DISCUSSION

Only the attempt to meet the crisis of parenthood, which had ended so disastrously for a mother in the patient's childhood, fully revealed the latent weakness of the ego-identity. One of the greatest crises in development faces a child whose impulses and fantasies have met those of an increasingly psychotic mother; a mother who subsequently disappears as though dead, but cannot be mourned because she is not dead. There has been a struggle against identification with this important early figure because of the ambivalence and trauma associated with her. This identification had, however, been carried in latent form, hidden and unintegrated. The childhood ego was too immature and had too little help from the subsequent environment to cope with this experience. Later experiences with significant adults were as though superimposed, but the whole could not be synthesized.

What early pregenital and oedipal material is revealed in the delusions, fantasies, and transference material of these patients? There is omnipotence and power, the magical ability to make people ill and die when they do not respond to one's wishes. This came true with the mother's illness that removed her from the home. There is the wish to be indulged and to be the only one. This involves hostility toward rivals and toward the mother for producing rivals. These destructive wishes also came true. We see evidences of the oedipal conflict, of wishes to displace the mother with the father. Mother was displaced, with the ensuing events sometimes representing a fight against the realization of this wish as illustrated in the case of Maria F., where a relative commented about the patient's relation to her father after the mother's hospitalization: "It was all right, but she didn't get a lot of affection—she thought he didn't like her, maybe *shouldn't* like her." In other cases, where the father kept the family together with the help of a housekeeper, we note a realization of the wish to have a special hold on the father.

Freud (8, 9), in distinguishing between neurosis and psychosis, emphasized that the problem for the psychotic lay in the disturbed relation between the ego and its environment. What major environmental realities trouble the patient now and how closely are these related to what the patient faced as a child? While this situation is complex, let us choose two factors: first, the interpersonal relationship involved between a potentially psychotic mother and her child; second, the importance of the "saga"[4] of psychosis in these families.

When we consider the influence of the psychotic mother on our patient, it will be objected that our patient had siblings who did not become psychotic and that these siblings were also subjected to the influence of a psychotic mother. Is it, then, this particular child who happened to inherit the mother's predisposition to mental illness?

There turns out, however, to be a reason why this child was an emotional target for the mother and why the other children escaped to a greater extent. Each of the patients who showed the age correspondence between a present child's age at her hospitalization and her own age at the mother's hospitalization had a special position in the family. Each was a first daughter. She might be an only child or she might be a first daughter though not a first-born child. From recent studies such as McArthur's (15), it is increasingly apparent that birth order is important. The older child is apt to be adult-oriented, serious, and sensitive while the younger child is more often peer-oriented, irresponsible, and gay. Parent-

[4] We are indebted to Dr. Lawrence Kubie who used the term saga in his discussion at the meeting of the American Psychoanalytic Association in December, 1956, of cases where a child had been repeatedly reminded of her mother's death.

oriented can mean more competitive with parents as well as more absorbed in their affairs.

There is evidence to indicate that a number of the psychotic mothers tended to have special symbiotic relationships with their daughters, our patients. In the case of Maria F., we saw that the symbiosis carried with it extreme ambivalence. The patient's daughter Priscilla was described as her mother's joy but also capable of driving her to distraction. She felt Priscilla was very much the way she had been as a child with her own mother. Another patient said her mother had seemed to depend on her to an unusual extent, so much so that she was "an old lady" when still a child; yet she also felt she was spoiled by her mother. A third patient recalled fear in relation to her mother since mother had attempted to strangle and choke her prior to being taken to the hospital. She felt she was the target for mother's hostility because she was the oldest and a girl. She stated that though she knew there were happy memories of her mother, she had never dared to think of them or of her mother at all because of the panicky feelings related to the fearful final days. This reaction reminds one of the first patient's fear when she recognized the symbolism of mother's violence in throwing the dolls into the fire. No wonder this area of identification was sealed off and remained unintegrated.

Anna Freud (7) states in regard to motherless and orphaned children that all the bogeys that had troubled their mothers' minds in the past were taken over; they reacted just the opposite from normal children by taking responsibility for overcoats, galoshes, and sleep. In identification with the temporarily or permanently lost mother, they substituted themselves for her by perpetuating the bodily care received from her. The motherless child tended himself in behalf of the mother who was gone, played "mother and child" with his own body.

In this connection Anna Freud is speaking generally of children's reactions to bereavement when a more normal mother is lost. What happens when a child has experienced a psychotic mother prior to the permanent loss? Bogeys were not only rubbers and sleep and overcoats but irrationalities, confusions, often destructiveness. Symptoms of an intensely disturbed interpersonal kind were inescapable. When a psychotic mother is experienced, the daughter cannot identify with the mothering the way Anna Freud's children do. She is bereft of this defense against the anxiety of separation because she must struggle against such an identification. It can be carried only in latent form, fought because of its frightening qualities and its alien character.

Under such conditions there has been a minimum of overt mourning for the lost mother. Our patients report a confusion of feelings such as loneliness, fear, and inability to comprehend, a feeling of desertion, shame over such a "different" mother, anxiety over their part in this tragedy.

With the lack of an ability to mourn we know that one mechanism of handling the loss is introjection of the lost object. The resulting sequence of depression was avoided by fixation, by remaining the child and avoiding responsibility. A developmental arrest occurred at the time of the loss both because of the trauma and because such a large segment of previous experience could not be integrated, but had to be avoided and denied.

One of the most persuasive factors in the life history of some of these patients is the saga of psychosis. Federn (6) remarks, "One learns from the psychoanalysis of adults that for the child the knowledge that a psychotic parent is, or was, hospitalized is as traumatizing or even more so, than living with such a parent." If, in addition, the patient has been reminded either subtly or openly of similarities between herself and her psychotic parent, the burden may indeed be overwhelming for the immature ego.

The following case illustrates the intensity of this factor.

Dorothy C. was the youngest of three children, the only girl. When she was 22 months of age her mother was permanently hospitalized. When her own daughter became 22 months of age, she was hospitalized. One month before entry the patient spoke about her fear of losing her mind like her mother and began recalling all the times she had been told she was like her mother and would end in the same way. She and her brothers were raised by the paternal grandparents. Her father, who visited infrequently, eventually remarried and lived in another city. The grandmother was a dominating woman, very severe with Dorothy and much less so with the boys. She gave Dorothy little or no affection, used corporal punishment almost daily until adolescence, and accused her of sexual delinquencies during childhood. The grandmother, who hated Dorothy's mother, frequently noted the similarities between her and her mother and predicted she would "end in the same way." The story was often repeated: "You were 22 months of age when your mother went away to the hospital."

Dorothy had completed two years of college when she married a fellow student. Before the wedding, her father reminded her that she had to tell her future husband about her mother's illness, and warned her that something of the same sort might happen to her after she had children. After marriage, for the first time in her life, Dorothy wanted to visit her mother in the hospital and said afterwards she began to suspect at this time that she was like her mother. Here, at the crisis of marriage, we note a beginning shift in her concept of her identity as she attempted to integrate the role of wife.

After the birth of the first child, a son, she experienced considerable nervousness. After the birth of her daughter, whom she named partly for her mother, she was again quite nervous. But this did not increase markedly until one month before admission when she became preoccupied with the similarities between herself and her mother, and became disoriented and delusional. She forgot her middle name, which was that of her mother. In the course of treatment she expressed much jealousy of her daughter's relation with her husband, guilt over her earlier sexual experiences with her brothers.

In this case we see that the saga, or repetitive story by the grandmother of Dorothy's likeness to her mother, had its effect. We may recall that the aunts in the case of Maria F. had similarly looked expectantly for signs of mental illness. In its broadest outlines, it is indeed the saga of psychosis that assists so profoundly in producing what Erikson terms a negative identity.

A fascinating illustration of the influence of the saga comes from Marie Bonaparte's report (1) after her analysis with Freud. Although this does not deal with maternal psychosis but with maternal death, it serves to underscore the effectiveness of a saga. In her account she reveals much rich material involving oedipal wishes toward her father (she was an only child and father did not remarry), but it is the saga that is of interest to us, here, a saga that must have been well conveyed since her mother died when Marie was one month old. Marie, who was named for her dead mother, was repeatedly told how her birth had been paid for by her mother's life. Throughout her childhood, she imagined she had really seen her dead mother. At 17 years of age she gradually became convinced that, like her mother, she had tuberculosis and that this fact was being kept a secret from her. Her mother had died at 22, and Marie expected that she, too, would die of tuberculosis at 22. Her symptoms began to mimic TB; she lost appetite and weight, and had frequent respiratory infections. At 20, the age at which her mother married, her illness became worse; she had a bloody mucus in the throat and began to waste away. Since her mother had died at 22, Marie felt she had

to pass this age before she would know whether she could live. Her sickness had the important function of discouraging her from marrying. If she did not marry, she would not become pregnant and therefore would not suffer her mother's fate. When she was 22, her father pointed out to her that it was high time she found a husband and forgot about her imaginary illness. Not only was her father telling her she must thus renounce him and her identification with her mother, but there was the clear fact that she had reached 22 and was still alive. From then on her symptoms began to wane. Here, then, we see a defense against repetition by avoiding the prescribed pattern that would carry out the saga and punish her for her guilt.

One of the patients in our group of 14, whose mother was permanently hospitalized when she was five, commented, "Mental illness was pushed into my head." What was "pushed" was the feeling that because the mother had become mentally ill the patient was destined for the same fate. This attitude, spoken as well as implied, was conveyed to her in her growing years, particularly by the aunt (the mother's younger sister) who raised her out of a sense of duty, with little warmth and with much resentment over the additional burden.

This role assignment represented a projected part of the remaining parent or parent-substitute dictated by the latter's ambivalence and anxiety. It has elsewhere (11) been pointed out how a parent can unconsciously direct his or her children into sibling rivalries that reproduce those from this parent's childhood. Johnson and Szurek (14) have stressed that many delinquent children and adolescents have experienced powerful suggestions from the parents to act out the repressed delinquent tendencies of the parents themselves. In the case of Dorothy, where the mother was lost at 22 months, we saw the grandmother's conviction about both mental illness and sexual acting-out communicated to the granddaughter. Both occurred.

One can also speculate as to whether there is an hereditary factor of ego weakness in these cases. Certainly if such combinations of mother and child with schizophrenia had not been carefully studied, they would immediately have been ascribed to innateness. We cannot assess this factor even with the information at our disposal. Though we have demonstrated that one child in the family can be singled out by the psychotic mother or by the subsequent guardian for a special relationship, who is to say whether there are not other first daughters of psychotic mothers who have been singled out for a special role and who have not succumbed to the later illness because they did not have a particular arrangement of genes?

What we can see and trace, however, is the immense contribution of certain environmental factors in the childhood of such patients. We begin to sense how much a particular position in the family, a special symbiotic relation with a sick mother or a disturbed substitute mother, a traumatic separation, a subsequent saga, and guilt, can exert an inexorable effect on the course of individual development.

What identity had the patient achieved in her adult life prior to reliving the old trauma? The childhood self had in large part remained on a pregenital level, with prominent oedipal elements. The early identifications associated with the ill mother were carried as an alien part of the ego. There were areas in which growth had occurred, but these were not integrated with the earlier, traumatic relationships. A "child identity" could be retained until parenthood. The patient's potential identification with her ill mother was revived with the birth of her child. Sometimes we see defenses against this, such as psychosomatic symptoms, acting out, or divorce. A case of ulcerative colitis as an anniversary symptom is reported by Bressler (3). The patient's mother had become psychotic when the patient was five years old and the pa-

tient began reliving this event when her daughter was five, with ulcerative colitis as the major and nearly fatal symptom.

The reaction at the anniversary of the childhood trauma is an indicator that an identification has been in process all along. The past has been reinstated, but it does not reach its malignant form until the anniversary of the old crisis. Identity diffusion occurs with the full impact of this terrifying period. The anniversary is the trigger. Throughout the chronic mother-daughter problem, there has been an unconscious projection and expectation in time. There is indeed an ability to foretell the future in many of these cases because the patient has been reliving a past experience and knows the outcome. She has projected onto the child the old relationship she had with her mother. These cases are related to some reported by Chapman (4) in a paper on the concept of nemesis in psychoneurosis; patients feel they are destined to repeat in their lives the pattern of a parent's life usually to a tragic end, due to profound guilt feelings.

At the time of the anniversay we have two mother-child entities where the patient is mother and child and where the patient's child is also mother and child. Our patients are competitors with their daughters as though they were peers. The power struggle and the oedipal rivalry are usually considered primarily a problem for the child, with the child at a disadvantage in competition with the parents. In these cases, however, the mother is competing with a child who is in a much more powerful position. The last time this situation occurred, a mother lost. With the anniversary age our patient, because of the reality of her position as mother, and because of her guilt, also loses. As Federn (6) stated, psychotic patients do not readily tolerate unconscious reversal of the oedipal situation in parenthood. We might add that the unconscious reversal of the oedipal situation in parenthood is sometimes the precursor of psychosis.

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CIVIL LIBERTIES AND MENTAL ILLNESS

Some Observations on the Case of Miss Edith L. Hough

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I

The following brief comments are intended to call attention to what I believe are inroads of serious import which organized psychiatry is making into the area of civil liberties. The significance of this encroachment transcends the specialized interests of psychiatry and jurisprudence, for it involves the most basic value of Anglo-American democracy, namely, the worth of the individual's autonomy and dignity. Cast in the context of current political and social events, it would seem that what the Western democracies can pit against the claims of opposing ideologies is not a high standard of living; nor is it the abstract notions of free enterprise, capitalism, or even the Christian ethic. What democracies, and *only* democracies, possess, and what can not be imitated by other ideologies—without themselves becoming democracies—is respect for the dignity and autonomy of the individual. Stripped of proud adjectives, this simply means that people must be taken seriously for what they do; and this implies holding them accountable for their actions.

Having argued elsewhere that psychiatric testimony concerning mental illness (as presently conceived) is distracting to judicial proceedings (7, 8), and that acquittal from a criminal charge by reason of insanity followed by commitment to a mental hospital constitutes a serious infringement of a person's civil liberties (4, 9). I shall turn, without further comment, to a recent case to illustrate and add to the points made previously.

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II

The case is that of Miss Edith L. Hough (2)[2]. The following are the salient facts, as abstracted from the records of her appeal to the U. S. Court of Appeals for the District of Columbia Circuit (Nos. 14923–24). On May 30, 1957, Miss Hough shot and killed a male friend who came to call on her to express his sympathy over the recent death of her father. The next day she was ordered to St. Elizabeths Hospital for determination of her competency to stand trial. She was subsequently found incompetent to stand trial and was committed to the hospital until restoration of her competency. In May, 1958, she was declared competent. She was tried for her offense—first degree murder—on July 10, 1958, and was acquitted by reason of insanity. She was then committed to St. Elizabeths Hospital.

On October 20, 1958, the Superintendent of St. Elizabeths Hospital filed in the District Court a certificate stating in part:

> "Miss Hough has now recovered sufficiently to be granted her conditional release from Saint Elizabeths Hospital pursuant to section 927 (e) of Public Law 313" (2, p. 2).

The District Court denied conditional release, whereupon the "patient" appealed to a higher court seeking reversal of this decision. The U. S. Court of Appeals for the District of Columbia Circuit heard the case and, on September 14, 1959, affirmed the decision of the lower court. In hearing the appeal, psychiatric testimony was obtained from Doctors Benjamin Karpman and Win-

[2] I am indebted to Judge David Bazelon for having called this case to my attention.

fred Overholser, and judicial opinions were rendered by Judges David Bazelon and Wilbur K. Miller. In the context of decision-making in an actual, real-life situation, the opinions and actions of the various participants become clearer than any statement, concerning psychiatry and law, that could be made in the abstract. My comments will be based on testimony and opinion recorded in the transcript of the decision rendered by the Appellate Court.

III

The first point on which I shall comment is the problem of acquitting a person of a crime and then committing him. Once he is acquitted, he must be considered (legally) innocent. If he is not so considered, the word "acquittal" and the deed it designates will lose their customary meanings.

Commitment of the insane—a complex, and in my opinion (5), highly questionable procedure as presently practiced—must now be scrutinized. Courts are legally empowered to commit people to mental hospitals, provided that certain conditions obtain. Illustrative is the case of a person who manifests such behavior as is considered patently deranged in our culture. A young man, for example, may become increasingly withdrawn and uncommunicative; he may stop eating and start masturbating in the presence of others. Sooner or later in the course of these events, the patient's family would very likely seek the aid of a physician (who may or may not be a psychiatrist). The latter would then make out the necessary papers *certifying* that the patient is in need of involuntary hospitalization. Finally, the judge under whose jurisdiction this matter falls would, in the ordinary course of events, order the patient *committed*.

Another type of situation in which people might be committed as mentally ill has traditionally been associated with the general area of criminal behavior. Without entering into the complexities of this matter, I wish to note only that according to the Durham Rule and its implementations (1, 3), persons charged with offenses but acquitted by reason of insantiy are committed to St. Elizabeths Hospital. If this practice were to be carried out *seriously* such persons would have to be treated as if they were *bona fide innocent*. This is required by the fact that they have been tried and have been pronounced *"not guilty* (by reason of insanity)." While the court has the right to order commitment, once a patient has been committed he comes under the jurisdiction of the hospital authorities. Hospital psychiatrists should be able to release the patient should they wish to do so. In cases of ordinary civil commitment, the court has no jurisdiction over the actions of the hospital staff vis-à-vis patients. To be more exact, the courts do have a say concerning hospital-patient relationships even in such cases, but this is essentially limited to giving the patient freedom. In other words, if the patient wishes to be released from the hospital over the opposition of the psychiatrists, he can, by availing himself of the appropriate legal safeguards, *e.g., habeas corpus*, enlist the aid of the court to gain his freedom. The reverse of this does not obtain! Should the hospital wish to release the patient, the court cannot interfere and keep the patient confined. It can not do this simply because commitment is legally justified—and this shows how poor this justification really is—by the psychiatric testimony of the physicians involved. Hence, if they (*i.e.*, the state hospital physicians) testify that the patient is sane, how can the court commit?

In the present case, it is to be noted that the court had the power not only to commit but also to regulate the patient's movements in and out of the hospital. This was in accord with a statute of the District of Columbia (D. C. Code §24–301 (e) Supp. VII, 1959). This meant, in effect, that the hospital functioned as an arm of the court.

It had no real autonomy, but was merely a subordinate body to the superordinate power of the courts. If a hospital superintendent and his staff can not discharge a patient from their "hospital" when they wish, then, I submit, they are but the functionaries of those who do have the power to make this decision.

All this points to the fact that hospitals functioning in such a fashion are, in fact, jails. But we can go further than this, for jails have a high degree of regulatory autonomy over their inmates. Parole boards, for example, can decide—within certain legally set limits—when prisoners may be released. The courts, once having passed sentence, can not interfere in this process. The regulations governing the release of mental patients from St. Elizabeths Hospital thus give the staff of this institution *less* jurisdiction over (some of) its "patients" than have jails over their prisoners.

We must infer from this that the courts, after having relinquished their responsibility to the psychiatrists for judging and sentencing criminals, have turned around and have arrogated to themselves the responsibilities of physicians and psychiatrists. This conclusion must be drawn from the fact that the courts take it upon themselves to decide when a person—officially designated a "patient," and one who has been acquitted of a criminal charge in a duly conducted trial, and is therefore "innocent"—may or may not be released from a place called "hospital." As matters now stand, psychiatric testimony in criminal trials—to the effect that the accused is mentally ill—makes it virtually unnecessary to have juries and judges, for acquittal follows almost automatically. Similarly, judicial authority of the type considered makes it virtually unnecessary, for patients of *this type* at least, to have psychiatrists and psychotherapists in mental hospitals—for it is the court, in the last analysis, that will decide when the "patient" is well enough to be released. The tragi-comedy that has been called "psychiatric testimony" has traversed a full circle: The psychiatrists who displaced the legal authorities (the latter having abdicated their responsibilities for decision-making of this type) (10), have, in their turn, been displaced by the legal authorities, who now function in the guise of psychiatrists and social therapists.

All this leads finally and inevitably to the psychiatrist's surrender of his professional responsibility. For, if a psychiatrist in charge of a patient—who is *not* a convicted criminal!—regards him, in his own best judgment, as ready to leave a hospital and assume the duties of a job, how can he, in his professional conscience, let a court tell him that this he can not do? What is the psychiatrist "treating" the patient for, anyway? To make him a good "prisoner?" The farcical, were it not tragic, character of the notion of mental illness (11, 12) is well illustrated by these impossible dilemmas into which psychiatrists and lawyers place themselves, each other, their patients, and their clients.

The peculiar legal condition of a person such as Miss Hough has not escaped the participants in this difficult affair. Judge Bazelon expressly affirmed that such a person is a "patient," not a "prisoner." The facts of the matter, however, vitiate the practical meaning of these terms. Judge Bazelon's words illustrate the crux of the problem:

> "Nothing in the history of the statute —and nothing in its language—indicates that an individual committed to a mental hospital after acquittal of a crime by reason of insanity is other than a patient. The individual is confined in the hospital for the purpose of treatment, not punishment; and the length of confinement is governed solely by considerations of his condition *and* the public safety. Any preoccupation by the District Court with the need of punishment for crime is out of

place in dealing with an individual who has been acquitted of the crime charged.

It does not follow, however, that the hospital authorities are free to allow such a patient to leave the hospital without supervision. We readily grant that periodic freedom may be valuable therapy. So, we suppose, may outright release sometimes be. But the statute makes one in appellant's situation a member of 'an exceptional class of people.' *Overholser v. Leach, supra*, 103 U. S. App. D. C. at 291, 257 F2d at 669. It provides generally, that the District Court have a voice in any termination of her confinement, whether unconditional or conditional" (2, p. 7).

There is an attempt here to circumvent the problem by creating the somewhat mystical entity of "an exceptional class of people." What is meant by this? Are these people who are "legally innocent but *really* guilty?" Or are these people who, by virtue of their actions, shall henceforth and forever after be considered second class citizens? Does this mean that we shall have two sets of laws, one for ordinary citizens and ordinary criminals, and another for the "mentally ill?" If these questions are answered in the affirmative—as they seem to be in this case—then surely we ought to ask: Is this in accord with the spirit and the letter of our Constitution, our Bill of Rights, and with the ethics of democracy?

Before bringing this discussion to an end, I wish to comment briefly on two other items found in this record. One is an opinion by Judge Wilbur K. Miller, stating:

> "It is, of course, much easier to believe that a sane person will not in the reasonable future be dangerous to himself or others than to believe that an insane person will not be" (2, p. 13).

Here is an ancient view, equating violence and insanity, dressed in slightly more modern garb. What is being asserted here, if anything? Both "insanity" and "dangerousness" are such vague terms that it is impossible to know what is being asserted by such a statement. But not only is this statement vague, worse, it is tautologous, for we habitually infer a condition of "insanity" from acts of violence. This was precisely the case in the present instance, for Miss Hough was considered legally sane until after she committed a murder. But if we infer insanity from violence, naturally we shall always expect violence when we speak of insanity, even though, in everyday life, the latter term is often used quite independently of whether or not a person is consider "dangerous."

In this connection, we must also note that the common-sense formulation of "insanity" propounded by Judge Miller seems to serve the function of enabling the observer —and this means all of us, and especially juries and judges—to wrestle with the problem of a person's so-called possible future dangerousness. At the very least, by codifying acts of violence as expressions of "mental illness" and some sort of irrationally (which, according to *certain* criteria, they might well be), we neatly rid ourselves of the task of dealing with criminal offenses as rational, goal-directed acts in principle no different from other forms of conduct.

Finally, I wish to call attention to a portion of Doctor Overholser's testimony. Being challenged by the attorney for the appellee to show reason why the patient should be released from the hospital, he was asked this question:

> "Now, if this woman, who has this major mental disease, were released conditionally into the community and met a great number of frustrations in adjusting herself in getting along, isn't there a probability or possibility that she might explode, so to speak, and even do harm to herself or to others" (2, p. 20)?

His answer was:

> "Well, there is that possibility with a great many people, some of whom have never been in mental hospitals. I can't

make any guarantee about permanence, or even about the conduct" (2, p. 20).

Here, it seems to me, Doctor Overholser spoke as a psychiatric scientist. As such, he could not predict with certainty, and surely could not guarantee, that this woman would not kill again. But if this is true, how can psychiatrists justify hospitalizing and "psychiatrically treating" someone whose "illness" appears to be mainly that she killed someone. Is being a murderer an illness? And if psychiatric treatment still leaves open the possibility of future crime, as obviously it must, then why use it as a *substitute* for legally codified imprisonment?

Does all this not mean that a logically simpler, and legally and psychiatrically clearer approach to a problem such as this might lie in treating persons in Miss Hough's predicament with the same dignity and firmness as we treat others confronted by serious problems? Why could she not be found guilty of a crime she obviously committed? Why could she not be imprisoned for a given term and, if necessary, given psychiatric help in jail? Is it not a truism that in a democracy, imprisonment (or loss of liberty) is justified only by conviction for a crime? But Miss Hough, and others in similar positions, were never convicted of a crime, but are, nevertheless, deprived of their liberty (6, 9). This is clearly done as a *preventive measure*! Herein lies, I think, the worst and most dangerous feature of this procedure: it establishes legal precedent, and hence a measure of sanction, for prophylactic imprisonment! Let us not forget that this social act has, and with good reason, been regarded as the hallmark of the totalitarian state. The legal restraint of a person justified by *what he might do* (in the future) is there used with the explicit aim of social reform. Although not explicitly formulated, and perhaps only as an unwitting and undesired side-effect, this tactic of preventive restraint seems to be implicit in the operations of the Durham Rule and its subsequent modifications and applications.

The merits and risks of preventive imprisonment—even if some choose to call it "hospitalization"—are well worth the attention of every informed and intelligent person. This was my reason for stating at the outset that many problems of psychiatry and law transcend the boundaries of these disciplines and rightly concern all the people of the land. Let us at least entertain the possibility that by engaging in certain modifications of social living—for this is what we are doing—we run the risk of squandering the greatest asset of our Nation and its distinctive form of government, namely, the autonomy, integrity, responsibility, and freedom of the individual.

IV

A recent decision rendered by the United States Court of Appeals for the District of Columbia Circuit was examined for the light it threw on some problems concerning crimes, psychiatry, and civil liberties. It was shown that acquittal by reason of insanity, followed by automatic commitment, seems to lead by easy steps to preventive jailing (hospitalization) of persons because of their alleged future dangerousness.

Increased psychiatric participation in the disposition of criminals seems to invite its corollary, namely, increased legal participation in psychiatric operations. We might raise the question: Do the questionable benefits of the Durham Rule (and its implementation) justify the risks of this "social therapy?" Could it be, perchance, that the cure, in this case, is worse than the disease? In other words, are the political and ethical risks of preventive jailing (preventive mental hospitalization) worth running, even if the psychiatric value of this measure were firmly established? (The psychiatric-scientific rationale of this procedure is hardly clear-cut or well established.) Personally, I hold that the value of formal psychiatric therapy for "criminals"

—under present medico-legal conditions—is, at best, highly questionable. But beyond this, I believe that even if this psychiatric-legal procedure could be shown to be highly efficacious in restoring offenders of a certain type to useful social existence (which is the most that even its proponents claim for it), I would doubt that, *in a hierarchy of values*, such therapy of a small group could be justified *if* its results could be achieved *only* at the cost of a significant reduction in the autonomy and dignity of the majority of the people. In any case, the problem of crime and "mental illness" should be cast in a much broader context, and should be scrutinized by many more people, than it is at present.

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PHYSICIANS' ATTITUDES TOWARD CHEMOTHERAPY AS A FACTOR IN PSYCHIATRIC PATIENTS' RESPONSES TO MEDICATION

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Previous studies have suggested that attitudes of hospital personnel toward tranquilizing drugs may be a significant factor in the process and outcome of drug therapy with psychiatric patients. Sabshin and Ramot (8), for example, carried out an exhaustive investigation of the attitudinal climate in their hospital and concluded that the staff's relatively unfavorable attitudes toward chemotherapy were contributing to patients' comparatively low rate of improvement under tranquilizing medication. Feldman (4) has reported a study in which pro-drug physicians were found to obtain better drug treatment outcomes than anti-drug physicians, a result which he interpreted as indicating the importance of attitudes. While Feldman did not apply refined statistical methods to the analysis of his findings, we have done so, and they were decidedly and significantly in the direction appropriate to his conclusion. The part that physicians' attitudes played in Feldman's study is not unequivocal, however, since drug dosage levels were not controlled. If one makes the reasonable assumption that physicians with more favorable attitudes toward tranquilizing drugs are likely to prescribe larger drug dosages than those with less favorable attitudes, Feldman's findings are subject to the alternative interpretation that they merely indicate the greater efficacy of higher levels of drug dosage rather than demonstrating the influence of attitudes *per se*. To test adequately the hypothesis concerning attitudinal effects on patient improvement, a situation is required in which the physicians' attitudes vary while level of dosage is held constant for all physicians.

Other research has found physicians' attitudes toward drug therapy to be related to the extent to which they utilized such treatment. Mason and Sacks (7), in a recent article, reported a significant positive correlation between attitudes toward chemotherapy of physicians at a Veterans Administration neuropsychiatric hospital and the proportion of patients for which each physician had prescribed drug therapy. With the widespread current use of tranquilizing medications in the treatment of mental illness, such a result would, of course, be rather difficult to duplicate, since few hospitalized psychiatric patients do not receive at least some medication. Another possible difference in use of medication by pro- and anti-drug physicians, as yet unexplored, is that of dosage level prescribed. As mentioned above, one might raise the question as to whether physicians favorably disposed toward tranquilizing drugs would prescribe larger medication doses than would those with less favorable attitudes.

The Veterans Administration's Cooperative Chemotherapy Project #3 (CCP#3) offered a setting suitable for research on the effects of physicians' attitudes. One of a series of nation-wide field experiments on the efficacy of various chemotherapeutic agents, CCP#3 investigated the effects of five phenothiazine-derivative, tranquilizing drugs. It consisted of a 12-week double-

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blind study, with a fixed progressive dosage period during the first four weeks of the study, followed by a flexible dosage period during the remaining eight weeks. The fixed dosage period met the requirement for investigating the relationship between physicians' attitudes and patient response, while the ability of physicians to vary drug level within rather broad limits during the flexible dosage period permitted an analysis of the relationship between physicians' attitudes and dosage level prescribed by them.

The following hypotheses were set forth to be tested.

1. Patients of physicians with more favorable attitudes toward the effectiveness of chemotherapy will show greater improvement under a presumedly effective, fixed, progressive dosage regimen than patients of physicians with less favorable attitudes toward drug therapy.

2. Physicians with more favorable attitudes toward the effectiveness of chemotherapy will prescribe larger drug dosages under a flexible dosage regimen than physicians with less favorable attitudes toward drug therapy.

METHOD

PHYSICIAN SAMPLE

Forty physicians from 16 VA hospitals participating in the VA Cooperative Chemotherapy Project #3 were utilized in the study.

PATIENT SAMPLE

Patients on whom data were obtained from CCP#3 consisted of 111 newly-admitted schizophrenic males under the care of the 40 physicians described above. Each patient was randomly assigned to receive a particular medication during the study. A more elaborate description of the overall CCP#3 patient sample from which the 111 patients were obtained can be found in an article by Casey *et al.* (1) and in the study protocol contained in the "Transactions of the Third VA Research Conference on Chemotherapy in Psychiatry" (11).

ATTITUDE MEASURE

A revised version of the scale previously constructed by Mason and Sacks (7) was used to measure attitudes toward the efficacy of the tranquilizing drugs in the treatment of mental illness. The initial form of the scale underwent additional refinement and standardization by the present authors, including rewording of some statements and an item analysis based on the responses of a group of 55 additional physicians from private, State, and Veterans Administration hospitals. The final form of the Likert scale (3) contained the 12 pro- and 12 anti-chemotherapy items which differentiated best between physicians with high and low overall scores in the standardization group. Responses to each item were scored on a one- to five-point basis, depending on the favorability-unfavorability of the item and the respondent's degree of agreement with it. Each physician's total attitude score was obtained by summing his scores for the individual items.

The split-half reliability coefficient for 40 CCP#3 physicians, corrected by the Spearman-Brown prophecy formula (5), proved to be +.92. The test-retest reliability coefficient for 18 such physicians, with a 7-month time interval between first and second testing, was +.83. These figures indicate that both halves of the attitude scale were measuring the same variable consistently and that attitudes toward chemotherapy were stable over time rather than of a transitory nature.

PATIENT RESPONSE MEASURE

The Total Morbidity score derived from the Lorr Multidimensional Scale for Rating Psychiatric Patients (6) was used to assess patient improvement. This score is an overall measure of psychopathology obtained by determining how much the patient's score on each of 11 scale factors deviates from a

normal score, then summing all such deviation—hence the "Total Morbidity" designation. Part of the ratings are based on clinical interview behavior while the remainder deal with ward behavior.

DOSAGE LEVEL MEASURE

The total number of drug capsules prescribed by each physician during the eight-week flexible dosage period for each patient under his care was employed as the index of drug dosage level.

PROCEDURE

The Attitude Toward Chemotherapy scale was administered to the CCP#3 physicians, who were then divided into two groups: those above and those below the median favorability of drug attitude (hereafter referred to as the More Favorable and Less Favorable group, respectively). Eighteen of the physicians filled out the scale both before the project and after its conclusion. The remaining 22 physicians were administered the scale only once, *i.e.*, after the completion of the project. The latter step was taken in an effort to increase the size of the physician sample. The before and after attitude scores of the first group of 18 physicians were highly correlated (+.83), indicating that the physicians would be categorized similarly as above or below the median on the basis of either their before or after score. Because of the high repeat reliability of the scale, we thought it feasible to combine the 22 additional physicians with the original 18 into one overall group of 40 subjects.

Each patient was rated on the Lorr scale just before the beginning of the fixed dosage period and again immediately after its conclusion four weeks later. The clinical interview ratings were made by a 2–3 person team of physicians and psychologists. They met and discussed their individual observations, then made a joint rating on each item based on their consensus concerning the patient's current status. The ward behavior ratings were made by a 2–3 person team of nurses and nursing assistants, who also discussed their individual impressions until they reached a group agreement. The difference in Total Morbidity score at these two times indicated the extent of the patient's improvement.

During the eight-week flexible dosage period, each physician varied drug dosage as he saw fit, within rather broad limits, in order to maximize therapeutic gain on the part of the patient. Upon completion of this phase, the total number of drug capsules prescribed for each patient was summed over the entire eight-week period.

STATISTICAL ANALYSIS

A 2×5 factorial design analysis of variance (2) was employed. The first variable was that of Physician's Attitude toward Tranquilizing Drugs, divided into those above vs. those below the median. The other variable was that of Drug, divided into five categories, since five different tranquilizers were evaluated in the study. The latter subdivision was made in order to determine whether physicians' attitudes played a consistent part over phenothiazine drugs in general or whether the effect of attitudes varied widely depending on what drug was being used. Since the number of physicians, and therefore patients under their care, differed slightly for some cells in the analysis, the correction for disproportionate subclass numbers described by Snedecor (9) was used.

RESULTS

PATIENTS' RESPONSES

Table 1 summarizes the analysis of changes in Lorr Total Morbidity score from before to after the fixed dosage period. Both Physician's Attitude and Drug proved to have a statistically significant effect on overall psychopathology. Patients of physicians with more favorable attitudes toward chemotherapy showed greater im-

provement (*i.e.*, diminution of overall pathology) than did patients of physicians with less favorable attitudes ($p < .025$), a result in the direction predicted from Hypothesis 1. The interaction between Physician's Attitude and Drug was non-significant, indicating that the superior improvement shown by the patients of physicians with more favorable drug attitudes was generally consistent over the five phenothiazine drugs rather than being true for only one or two such medications. Findings for the drug variable will not be dealt with in this paper, since they fall within the province of the CCP#3 study and will be reported at length by that project in separate publications.

DOSAGE LEVELS

Table 2 summarizes the results of comparisons between More Favorable attitude and Less Favorable attitude physicians with respect to the amount of medication they prescribed during the flexible dosage phase of CCP#3. The result for the variable of Physician's Attitude was in the direction predicted from Hypothesis 2, in that More Favorable physicians prescribed larger dosages than Less Favorable physicians. The probability value for this finding just missed the .05 level of statistical significance set for the study, falling between the .10 and .05 level instead. A result at such a probability level can be considered as supportive but not conclusive evidence with respect to Hypothesis 2. Additional research evidence would be necessary before the hypothesis could be regarded as having been clearly confirmed. The Attitude by Drug Interaction proved to be insignificant, reflecting a consistent tendency for the More Favorable physicians to prescribe larger dosages no matter which phenothiazine drug patients were receiving.

DISCUSSION

The results of the study clearly substantiate the first hypothesis of a relationship between physicians' drug attitudes and patients' improvement under medication. They also provide some, though less clear-cut, support for the second hypothesis concerning a relationship between physicians' attitudes and drug-dosage level as well. From these results, it appears that Feldman's findings might have been due to a combination of attitudinal effects *per se* plus the possibility of an effect of differing drug-dosage levels prescribed by physicians with different degrees of favorability toward chemotherapy.

The question could conceivably be raised as to the extent to which change in Lorr Total Morbidity score should be considered an unbiased, objective estimate of patient improvement. It might be argued that the physician's attitude toward drug therapy could have biased the Lorr scale score results, since he was a member of the psychiatric team making some of these ratings. Such a line of reasoning could cite as support studies such as that of Thorpe and Baker (10), which found that attitudes of hospital personnel led to their reporting differential improvement from that perceived

TABLE 1

Analysis of Variance of Lorr Total Morbidity Score Changes During Fixed Dosage Period

Source of Variation	df	Mean Square	F-ratio	Probability Level
Physician's Attitude	1	1069.34	5.82	$<.025$
Drug	4	653.04	3.55	$<.025$
Interaction	4	309.90	1.69	Not signif.
Individuals	101	183.70		

TABLE 2

Analysis of Variance of Dosage Levels Prescribed During Flexible Dosage Period

Source of Variation	df	Mean Square	F-ratio	Probability Level
Physician's Attitude	1	13,759.62	3.34	$<.10$
Drug	4	6,235.62	1.51	Not signif.
Interaction	4	1,230.58	<1	Not signif.
Individuals	101	4,125.37		

by outside, objective observers for the same patients. There is, however, some rather clear incidental evidence against such a possibility in the present instance. In addition to participating in the Lorr scale pooled ratings, each physician filled out at the same time intervals a schedule which required a clinical estimate of various broad aspects of the patient's psychiatric status. In this schedule was an item concerning change in mental condition and a second item dealing with changes in severity and number of symptoms. For these two items, the physician was required to compare the patient's condition at the time of the rating with what it had been at a previous specified time. Such items offered the physician's attitude toward chemotherapy a maximum opportunity to bias his ratings. The items were couched in comparative rather than absolute terms; the physician was the sole rater using that schedule for any given patient; and the rating criteria were of a global nature. The Lorr scale, on the other hand, required absolute ratings; the physician was required to reconcile his ratings with the remainder of the psychiatric team in arriving at a consensus rating, and the rating criteria were specific in terms of symptomatology.

An analysis of variance was performed for each of the above two items from the clinical estimate of psychiatric status schedule. Uniformly non-significant effects were obtained for Physician's Attitude and for the interaction between Physician's Attitude and Drug. This indicates that the ratings of changes in patients' psychiatric status by physicians with more favorable attitudes did not differ from those by physicians with less favorable attitudes. The Drug variable proved significant for both items so that insensitivity of the measure does not seem to account for the lack of significance of Physician's Attitude. Such findings make it seem quite unlikely that the physicians' attitudes would have markedly biased their Lorr scale judgments or, in turn, the pooled Lorr ratings. Nevertheless, a future study, with completely independent raters assessing the patients' condition, would be useful to eliminate even the remote possibility of such an influence on the findings. There is also a need for further investigation in order to establish the limits to which the results of the present study may be generalized. Other types of patients, different samples of physicians, different hospital settings, other drugs, and a variety of dosage levels could thus be tried.

The Lorr scale findings regarding physicians' attitudes and patient improvement raise an interesting question: What is the means by which the physician's attitude is transmitted to the patient? Attitudes, of course, do not exist as disembodied entities, nor do they make their influence felt in a vacuum. They must somehow be communicated by those who hold them to those who are influenced by them. It would be interesting to pursue the topic further and to determine what communication channels to the patient are the means of attitude transmittal.

SUMMARY

The attitudes toward tranquilizing drugs of 40 physicians from 16 hospitals participating in a nation-wide VA Cooperative Chemotherapy Project were measured by means of a questionnaire of the Likert type. Those who scored above the median for this sample were designated more favorable and those who scored below the median less favorable in their attitude toward the drugs.

Changes in Total Morbidity scores on the Lorr Multidimensional Scale, administered before and at the end of a fixed progressive dosage period of four weeks, were computed for 111 male schizophrenic patients under the care of the 40 physicians. Each patient had been randomly assigned to receive one of five phenothiazine medications.

Dosage levels prescribed by the 40 physicians during an eight-week flexible dosage period were computed.

During the fixed progressive dosage period, patients of physicians with more favorable attitudes showed significantly greater decrease in Total Morbidity score on the Lorr scale than did patients of physicians with less favorable attitudes. The interaction between Physician's Attitude and Drug was non-significant, indicating consistently greater improvement over the five drugs for patients of the physicians who had more favorable attitudes.

During the flexible dosage period, dosages prescribed by more favorable physicians tended to be higher than those prescribed by physicians with less favorable attitudes, although the differences did not quite reach the five per cent level of significance. The interaction between Attitude and Drug was again non-significant, indicating that the tendency of more favorable physicians to employ higher dosage levels was consistent over drugs.

These results are discussed in terms of the possibility of bias in rating the patients' condition. This study needs to be replicated with other types of patients, in different settings and with other kinds and dosage levels of drugs.

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SEXUAL NORMS IN A PSYCHIATRIC POPULATION

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The etiology of the bulk of the disorders seen by psychiatrists remains obscure. Perhaps because of this a plethora of theories exist as ad hoc explanations of these disorders. Prominent psychoanalytic theorists such as Fenichel and Freud (1, 3) have directed their attention to the affectional life and more particularly to those experiences which they believe shape the attitudes to and subsequently the behavioral expression of the sexual function. These theorists, and many others, assume an innate sexual drive or an inborn impelling force towards sexual action. It is further assumed, with considerable evidence in support (2) that this drive, in terms of its object, is relatively nonspecific. The survival and effective functioning of the human group requires, however, that the drive become highly specific in terms of its object, namely that it should take expression at a particular time in life, in relation to an appropriate opposite-sexed person, under the circumstances of matrimony and with a time frequency consonant with the accepted standard of the particular society. It is assumed that this change in specificity is largely contingent upon the human being's undergoing certain kinds of learning experiences in his social relationships as he develops from infancy to adulthood. It is postulated that certain undesirable experiences will result in inhibition of the direct expression of the drive. Since the drive is innate and cannot entirely disappear, it is believed that it gains indirect expression in the form of the symptoms manifested by those persons classified as psychoneurotic and non-organic psychotic. It is postulated (1) that other undesirable experiences result not in inhibition but in deflection of the drive to socially unacceptable objects. These persons, classified as impulse neurotics and pathological personalities, direct their sexual drive towards fetish objects, towards their own sexual organs or towards humans of their own sex or other human or nonhuman objects, culturally unacceptable or biologically inappropriate.

These theories would lead one to suppose that the sexual life and practices of a psychiatric patient population would differ considerably from a nonpsychiatric population. To test this hypothesis, information was collected on some aspects of the sexual behavior of a sample of patients who were receiving out-patient psychotherapy. Data so derived were compared with similar data collected by Alfred Kinsey (4, 5) and associates on a large sample of a nonpsychiatric population.

METHOD

The sample consisted of 100 male and 108 female patients who were consecutive admissions to an out-patient psychotherapy unit. All patients were part of a larger study of factors affecting change in patients undergoing psychotherapy. The term consecutive must be modified in the sense that the patients had to conform to the criteria of selection for the larger study. Thus none had I.Q.'s below 80. None had a language problem that constituted a barrier to completing the tests. None was acutely excited or had brain pathology.

The information was collected by means of an individual questionnaire. In each case a reliability check of sorts was made by consulting with the individual therapist. The questions asked were as follows:

1. Have you ever had sexual intercourse?
2. At what age did you first have sexual intercourse?

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3. Have you had intercourse with more than one person?
4. With how many people have you had intercourse? a) Before marriage: b) After marriage.
5. Have you generally found sexual intercourse satisfying?

Data regarding age, age at marriage, and educational attainment, were obtained at the same time. In addition, each case history was reviewed and the patient classified under one of the following diagnostic categories: psychoneurosis, character disorder, affective disorder, schizophrenia, undiagnosed. The results were tabulated and statistical comparison made with the well-known data reported by Kinsey *et al.*

RESULTS

The results are collated in a series of accompanying tables.

FEMALE

Accumulative incidence of premarital coitus: Comparison of the total samples does not reveal a significant difference in the incidence of premarital coitus nor in the number of partners involved. In both groups of females, approximately half reported experiencing premarital coitus and of these about half experienced it with more than one partner. When the data are arranged by age and education, however, differences do appear (Tables 1 and 2). The psychiatric population began its premarital coital activity at a significantly earlier age than the nonpsychiatric, except in the case of those individuals who subsequently were to go on to college.

Accumulative incidence of extra-marital coitus: The incidence of extramarital coitus in the nonpsychiatric population is reported as 26 per cent by the age of 40. The overall incidence in the psychiatric group was 31 per cent. The size of our sample prevented us from calculating our results only on those patients who had attained the age of 40. Could we have excluded persons under forty, the presumption is that the incidence of extra-marital coitus would be significantly higher in the psychiatric group. In both groups, the greater the premarital experience, the greater is the likelihood that the person who has extra-marital coitus will have it with more than one partner.

Sexual satisfaction: Landis *et al.* (6) interviewed 44 normal married women and states that 38 per cent reported coitus satisfying and usually accompanied by orgasm. A further 32 per cent found coitus pleasant but rarely achieved orgasm. In our sample 57 per cent reported that sexual intercourse was generally satisfying. Interpretation of this difference is difficult since it is by no means certain that the same measures of satisfaction were used.

TABLE 1

Females—Age and Premarital Coitus: Accumulative Incidence

Age	Out-Patient Clinic (%)	Kinsey (%)	X^2	$p<$
0–15	10	03	18.07	.001
16–20	44	20	33.32	.001
21–25	60	33	24.55	.001

TABLE 2

Females—Accumulative Incidence: Premarital Coitus in Relation to Age and Education

Age	Education: 0–8				Education: 9–12				Education: 13 plus			
	O.P.D. (%)	Kinsey (%)	X^2	$p<$	O.P.D. (%)	Kinsey (%)	X^2	$p<$	O.P.D. (%)	Kinsey (%)	X^2	$p<$
0–15	14	18	.27	N.S.	11	05	3.55	N.S.	0	02		N.S.
16–20	50	25	6.53	.02	51	26	14.4	.001	17	20		N.S.
21–25	82	26	19.38	.001	72	37	21.45	.001	53	39		N.S.

Diagnosis: Our sample of women contained: psychoneurosis, 24 per cent; character disorder, 50 per cent; affective disorder, 10 per cent; schizophrenia, 12 per cent; and undiagnosed, three per cent. No diagnostic group contributed disproportionately to the reported incidence of premarital coitus.

MALE

Accumulative incidence of premarital coitus: Comparison of the total samples reveals a lower incidence in our sample than in Kinsey's nonpsychiatric population. Kinsey's material does not report the size of the total sample, and it is therefore impossible to determine the level of significance of the difference (Table 3). This difference is explained by the later age at which the psychiatric population began its premarital activity. If marriage is delayed beyond the age of twenty, the differences between the two groups disappear. In both groups, if marriage is delayed until the age of thirty, approximately 90 per cent of males will have experienced premarital coitus. When the data are arranged according to educational level (Table 4), it is clear that in both groups the incidence of premarital coitus declines as educational attainment rises. There is no significant difference in the incidence between the two groups of subjects of elementary education. In the younger age groups, the more highly educated patients in the psychiatric population were found to be significantly less active than their counterparts in the nonpsychiatric population.

TABLE 3

Males—Age and Premarital Coitus: Accumulative Incidence

Age	Out-Patient Clinic (%)	Kinsey (%)	X^2	$p<$
0–15	16	39	21.47	.001
16–20	54	73	16.46	.001
21–25	76	83	2.46	N.S.
26–30	91	86		N.S.

Accumulative incidence of extra-marital coitus: The incidence reported by Kinsey for his "normal" population, is 50 per cent by the age of 40. The overall incidence in the psychiatric group is 38 per cent. It is presumed that no significant difference would be found between the two groups, had the size of our sample allowed us to use only married males of age 40 or more.

Diagnosis: By diagnosis, our male sample consisted of: psychoneurosis, 21 per cent; character disorder, 46 per cent; affective disorder, 10 per cent; schizophrenia, 15 per cent; and undiagnosed, seven per cent. As in the females, the psychiatric diagnosis did not contribute to increasing our understanding of the incidence of premarital coitus: no category contributed disproportionately to the incidence.

DISCUSSION

The difference found in the reported incidences of premarital and extra-marital coitus between this sample of psychiatric patients and a sample of nonpsychiatric subjects can be summarized as follows.

TABLE 4

Males—Accumulative Incidence: Premarital Coitus in Relation to Age and Education

Age	Education: 0–8				Education: 9–12				Education: 13 plus			
	O.P.D. (%)	Kinsey (%)	X^2	$p<$	O.P.D. (%)	Kinsey (%)	X^2	$p<$	O.P.D. (%)	Kinsey (%)	X^2	$p<$
0–15	33	42	.83	N.S.	13	45	16.67	.001	04	10		N.S.
16–20	72	83	1.92	N.S.	62	75	3.23	N.S.	27	44	3.19	N.S.
21–25	91	90		N.S.	75	84	1.39	N.S.	62	64		N.S.
26–30	96	94		N.S.	94	84		N.S.	93	68	3.38	N.S.

In neither sex was there a relationship found between diagnostic category and incidence of pre- or extra-marital coitus.

In females, the overall incidence of premarital coitus is the same in both groups. In comparisons of the elementary school-educated members of both groups, the psychiatric subjects are more sexually active at an earlier age than their nonpsychiatric counterparts. The incidence of extra-marital relations is higher in the psychiatric population.

In males, except for the elementary school-educated, the psychiatric subjects appear to begin their premarital coitus at a later age than their nonpsychiatric counterparts.

Objections may be raised to the use of the Kinsey material as basic criteria for the sexual behavior of a nonpsychiatric population. It is entirely possible, too, that norms in a Canadian culture may be somewhat different from those in the U.S. It is also entirely possible that the data obtained by Kinsey were of questionable reliability. The psychiatric subjects' responses in this study were checked by the individual therapists: This, of course is no guarantee of accuracy, but Kinsey had no such reliability check. Anecdotal belief has it that females characteristically underestimate their sexual activities and that males overestimate. If this in fact is true and did happen in Kinsey's study, the differences found in this investigation would certainly be lessened.

If the differences found are valid, they do suggest that males who subsequently become psychiatric patients arrive at sexual maturity with attitudes to coitus that are inhibiting to its expression. By the age of 30, however these attitudes have changed and now conform to those of the nonpsychiatric population. Thus general support is given to Freud and others who postulate unresolved maternal attachments in male psychiatric patients, attachments which they suggest inhibit genital expression. Our findings further suggest that females who subsequently become psychiatric patients and who do not go on to college, arrive at sexual maturity with less inhibiting attitudes to coitus than their nonpsychiatric counterparts. These attitudes are persistent, as reflected in their increased likelihood to have extra-marital coitus. Psychoanalytic theorists have generally predicted lessened sexual inhibition in certain character disorders but increased sexual inhibition in the psychoneuroses. This study gives no support to those who presume differing sexual patterns for differing diagnostic categories. In particular, the often-heard assertions that schizophrenics are more inhibited than other types of patients, or that pathological personalities are less inhibited, receive no support.

SUMMARY

Distorted or unusual attitudes to the sexual function have been implicated by psychoanalytic theorists in the etiology of the bulk of the psychiatric syndromes. To test this hypothesis, the writers assumed that these attitudes would be reflected in premarital and extra-marital patterns of sexual behavior. Accordingly, information was collected on these patterns on a sample of more than two hundred psychiatric patients and compared with the information available on a nonpsychiatric population. The study gives some support to the hypothesis.

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BRIEF COMMUNICATION

SERUM PHENYLALANINE IN SCHIZOPHRENIA: BIOCHEMICAL GENETIC ASPECTS

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INTRODUCTION

Taking a biochemical approach to schizophrenia, investigators have suggested that various metabolic abnormalities are present with respect to amines, amino acids, and aromatic compounds (12, 19, 20). Conversely, a genetic point of view toward schizophrenia, taken by Kallman (9, 10), cites impressive data concerning hereditary mechanisms in psychoses.

Correlating these two approaches to schizophrenia is possible, using the work of some American investigators in the field of hereditary diseases. Hsia and co-workers have described a test which detects carriers of phenylketonuria (7, 8), an inborn error of metabolism with associated mental deficiency. The phenylketonuric patient presumably lacks a normal complement of a specific enzyme in the liver, phenylalanine hydroxylase.

Carriers of phenylketonuria (heterozygotes for the phenylketonuric gene) can be detected by a slight peculiarity of phenylalanine metabolism which suggests a subnormal amount of phenylalanine hydroxylase, and an amount between that of normal individuals and of phenylketonurics. Their plasma levels of phenlyalanine, both fasting and after phenylalanine loading tests, are elevated above normal.

Phenylalanine is an essential aromatic amino acid which is a precursor of many biologically active substances, including the catecholamines and thyroxine. It also has inhibitory effects on several naturally occurring enzyme systems, including 5-hydroxytryptophan decarboxylase, which is important in serotonin metabolism (2, 14). The exact biochemical mechanism for the central nervous system abnormalities in phenylketonuria has not been defined, but the primary suspect is phenylalanine or one of its metabolic derivatives.

A possible implication from these findings is that the heterozygote, with only slightly altered phenylalanine metabolism, might have subtle detrimental influences exerted on the central nervous system. This thought is more provocative when one notes an increase in psychoses in relatives of phenylketonurics (13, 15, 17) as reported by work of several investigators.

If, indeed, a correlation exists between phenylalanine metabolism and mental disorder, then one might expect to find a higher incidence of carriers of phenylketonuria in a psychotic population than in a normal group. Lippman (11) made a study of fifty schizophrenic patients to determine the number of carriers of phenylketonuria but obtained equivocal results due to the incomplete specificity of the test for heterozygosity.

To discover whether phenylalanine metabolism might be involved in the schizophrenic process, with possible biochemical genetic overtones, a study of forty chronic schizophrenic patients was undertaken.

MATERIALS AND METHODS

The patients utilized were diagnosed as schizophrenic at the Osawatomie State Hos-

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pital. Thirty-three men and seven women whose ages ranged from 25 to 73, were used. No treatment was given for at least two weeks prior to obtaining blood samples.

The controls, 12 men and three women, were staff members and employees of the Osawatomie State Hospital. Their age range was 17 to 56. These individuals ate at least one meal a day which was identical to the patients' diet.

Chemical determinations: Fasting serum phenylalanine was determined using a modification of Hsia's (6) modification of the method of Udenfriend and Cooper (18), utilizing the phenylalanine decarboxylase of Streptococcus faecalis.[2] Hsia's procedure was altered: Serum was used instead of plasma, a larger aliquot of deproteinized serum was added to the incubation mixture (the total volume was kept at 1.5 ml.), and the time of incubation was three hours.

Procedure: Fasting blood samples were taken in the morning and the serum separated by centrifugation. The serum was deproteinized on the day of collection or the following day. Some deproteinized samples were stored at −15°C for a period up to a week before chemical determinations were made.

RESULTS

The results for the patient and control groups are tabulated in Table 1. The mean fasting serum phenylalanine value for the controls was 1.88 mg per cent. The corresponding value for the patients was 2.65 mg per cent. The difference between these two values was found to be significant at the .003 level when analyzed using the t-test with a one-tail hypothesis.

An analysis of the various diagnostic subcategories of schizophrenia with respect to phenylalanine levels showed that all except the mixed type had values significantly greater than the controls. These results are shown in Table 2.

[2] The phenylalanine decarboxylase used was obtained from Worthington Biochemical Corporation, Freehold, New Jersey.

TABLE 1

Summary of Results: Patients and Controls

	N	Mean Phenylalanine mg per cent	Standard Error of Mean
Patients	40	2.65	0.16
Controls	15	1.88	0.12

$t = 2.91$ $p = .003$.

TABLE 2

Results: Schizophrenia Subcategories

Subtype	N	Mean PA	t	p
Catatonic	18	2.91	3.36	0.001
Hebephrenic	4	2.48	2.22	0.05
Mixed	3	1.97	0.29	0.39
Paranoid	8	2.56	1.88	0.05
Simple	7	2.47	2.69	0.01

DISCUSSION

The value of fasting serum phenylalanine obtained for the normal group, 1.88 mg per cent, falls within the range reported by several investigators (1, 4, 16), but is slightly higher than that reported by Hsia (6). However, the previous values were obtained with plasma, while this work was done with serum. There are no reports in the literature of serum values determined with the enzymatic decarboxylation method.

The breakdown into clinical subtypes did not reveal any metabolic differences. All the subtypes, except the mixed type, showed phenylalanine levels significantly greater than the normal group. However, the number of subjects in the subgroups was not large enough for definitive evaluation.

If the proportion of heterozygotes with respect to phenylketonuria in a schizophrenic population is greater than that in a normal group, one would expect the mean level of fasting serum phenylalanine to be greater in the former group than the latter. When this hypothesis was tested in the present study (one-tail test), a level of significance of .003 was obtained. This would

indicate that a peculiarity of phenylalanine metabolism is indeed present in schizophrenia.

The precise answer to the genetic question of heterozygosity for phenylketonuria, of course, has not been specifically answered. Since no known heterozygotes were available to the investigator for the purpose of establishing control levels with the method used, a strict delineation of heterozygotes could not be obtained. With known heterozygotes for controls and with more refined methods for determining heterozygosity (3, 5), the genetic factor could be elucidated.

It seems likely that, as further biochemical peculiarities in schizophrenia are discovered, the application of biochemical genetic knowledge will provide more clues for the understanding of this mysterious disease.

SUMMARY

A study of the fasting serum phenylalanine levels of forty chronic schizophrenic patients and fifteen normal controls was undertaken.

The mean value obtained for the patients was 2.65 mg per cent; for the controls, 1.88 mg per cent.

A t-test for the significance of the differences gave a p value of .003.

Within the clinical subtypes of catatonic, hebephrenic, mixed, paranoid, and simple, only the mixed type did not show a significantly elevated level of phenylalanine.

The significance of the results and the importance of the biochemical genetic approach to mental disorder are discussed.

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BRIEF COMMUNICATION

PYRIDOXINE DEFICIENCY IN CHRONIC ALCOHOLISM

FINN LUNDE, M.D.[1]

Hastings State Hospital receives all committed alcoholics from the State of Nebraska. In 1958 this accounted for 402 male admissions.

Less than half of these patients were transferred from other hospitals where they had been treated during the acute phase of their recovery; most of them were admitted directly to the State Hospital. The patients in the latter group enter the hospital after long periods of drinking, grossly intoxicated or in delirium tremens, with a history of inadequate food and vitamin intake, thus leaving theselves vulnerable to the effects of various nutritional deficiencies.

The routine treatment of these patients includes use of large doses of various vitamins, mainly of the B-complex. Among these vitamins the importance of B-6 or Pyridoxine is probably the least well known. Reports of its use in the treatment of acute alcoholism have been published; some conclude that there was no specific effect of Pyridoxine (1, 3, 7), although one report seems to indicate a calming effect (5).

Its use in "Rum fitters" has been reported (4). This study also presents biochemical evidence of Pyridoxine deficiency in these patients.

The reports of increased neuromuscular irritability, startle response and convulsions in children fed a Pyridoxine deficient diet (2, 6), and the findings of various neuropathies in patients given Pyridoxine antagonists, led us to postulate the hypothesis that Pyridoxine deficiency is a significant factor in the pathogenesis of alcohol-neuropathies and withdrawal seizures.

Since a large number of patients in whom one would expect to find evidence of such deficiency was available, an attempt to test this hypothesis was made. This paper reports the findings of this study.

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METHOD

The patients selected for this study were all committed male alcoholics with a history of excessive alcohol consumption and inadequate food intake for at least three months prior to admission. None of them was known to have epilepsy. They were either grossly intoxicated or in Delirium Tremens on admission. The groups were not matched for age, intoxication or delirium.

Except for the different amounts of Pyridoxine given to the patients in the different groups as described below, treatment was otherwise identical.[2]

[2] The routine was:

a) Promazine 200 mg. orally or 100 mg. intramuscularly given on admission, then half this dosage was continued four times daily until the patient was sober or out of delirium.

b) Thiamine hydrochloride 100 mg. intramuscularly daily.

c) 2 cc. intramuscularly on admission and twice daily for 5 days of an injectable multivitamin preparation containing per cc.:

Thiamine hydrochloride	10 mg.
Riboflavin	2 mg.
Niacinamide	100 mg.
Pyridoxine hydrochloride	5 mg.
Calcium pantothenate	5 mg.

d) An oral multivitamin preparation ("Clusivol") given three times daily as tolerated. Two capsules contain:

Vitamin A	25,000 U.S.P. Units
Vitamin D	1,000 U.S.P. Units
Vitamin C	150.0 mg.
Vitamin B_1 mononitrate	10.0 mg.
Vitamin B_2	10.0 mg.
Vitamin B_6	1.0 mg.
Panthenol, equivalent to of calcium pantothenate	2.0 mg.

TABLE 1

Summary of Results

	With Pyridoxine	Without Pyridoxine
N: Patients with seizures	1	7
N: Patients without seizures	22	16

The sample consisted of two groups. The first 20 consecutive patients were all given 100 mg Pyridoxine daily in addition to the basic routine, and the results were compared with previously admitted patients.

In the second group of 46 patients, alternate patients were given 100 mg Pyridoxine daily and the rest served as controls.

A preparation containing equal amounts of Pyridoxine and Thiamine was used. The control group received Thiamine only. Thus the number and gross appearance of the injections were the same in both groups.

The patients were under 24 hours observation. The only criterion used in evaluating the effect was the presence or absence of seizures. This is held to be a very reliable criterion, as the observations were made by trained, experienced hospital personnel uninformed about the treatment used in each patient.

Vitamin B_{12} with intrinsic factor concentrate	⅓ U.S.P. Unit
Folic acid U.S.P.	1.0 mg.
Nicotinamide	100.0 mg.
Vitamin E*	1.0 I.U.
Biotin	0.1 mg.
Lysine hydrochloride	50.0 mg.
dl-Methionine	25.0 mg.
Iron*	50.0 mg.
Calcium*	200.0 mg.
Phosphorus*	154.0 mg.
Copper*	1.0 mg.
Cobalt*	0.1 mg.
Manganese*	1.0 mg.
Iodine*	0.15mg.
Potassium*	5.0 mg.
Zinc*	1.2 mg.
Magnesium*	6.0 mg.

* Supplied as d-a-tocopheryl acetate concentrate, ferrous sulfate, dicalcium phosphate, copper sulfate, cobalt sulfate, manganous sulfate, potassium iodide, potassium sulfate, zinc sulfate and magnesium sulfate.

RESULTS

In the first group of 20 consecutive admissions all were given Pyridoxine. None of them had seizures. This compares with the usually expected frequency of 25 per cent with seizures.

In the second group of 46 patients, only one of those who received Pyridoxine had seizures[3] compared with seven in the control group, as shown in Table 1. These results are significant at the .02 level, using the chi-square test of independence in a contingency table.

DISCUSSION

These findings support the hypothesis that a significant deficiency of Pyridoxine can be found in chronic alcoholism and that this deficiency is a significant factor in withdrawal seizures. A follow-up study with biochemical testing of a similar group of patients will be arranged.

Since all patients in this study received 20 mg. daily in the routinely given multivitamin preparation without any effect on the frequency of seizures it would appear that the dose required to effectively treat the deficiency must be larger, probably around 100 mg. per day.

Since Pyridoxine is known to be a necessary co-enzyme in the metabolism of tryptophane and deficiency of this vitamin leads to changes in tryptophane metabolism, there may be a common biochemical basis for the alcoholic psychoses and some of the experimentally induced psychoses.

SUMMARY

100 mg Pyridoxine was added to the routine treatment of two groups of male patients. They all had a long history of continued, excessive alcohol consumption and deficient vitamin intake. None was epi-

[3] This man, who was found to have had two seizures before admission, suffered an attack of gout five days after admission. No evidence of uremia was found.

leptic. In the first group of 20 consecutive patients all were given Pyridoxine, none of whom had seizures, as compared with a usual frequency of 25 per cent.

In the second group of 46 patients, every other one was given Pyridoxine, the rest serving as controls. Only one patient in the treated group had seizures as compared with seven patients in the control group. This difference was found to be statistically significant at the .02 level of confidence.

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BRIEF COMMUNICATION

A HYPNOANALYTIC NOTE ON A MEDUSA'S HEAD DREAM

JEROME M. SCHNECK, M.D.[1]

Current developments in hypnoanalysis offer opportunities for the investigation of favorable extensions in the practice of psychotherapy, additional substantiation of psychoanalytic theories and concepts, formulations of new theories and concepts pertaining to treatment and to personality development and functioning, and elaboration of observations noted during the growth of psychoanalysis. Many illustrations are available to substantiate these comments. They may be found in journal publications and in books (5, 6). In the realm of symbolism, to cite only one example, a hypnoanalytic observation was offered recently on the heart as a phallic symbol (4). In the present communication I should like to extend a comment made by Freud some time ago on the psychological significance of the mythological Medusa's head, and to supply briefly a case setting where none was furnished in Freud's short article (3).

A 24 year old patient recaptured, during a hypnoanalytic session, a Medusa's head dream at the age of seven. His ability to retrieve it was consistent with his general hypnotic functioning in that phase of treatment when meaningful experiences, emotions, and interpersonal relations of early years were reactivated in content and aura. The facilitation of such recall through hypnosis is often one of its potential benefits. This patient's childhood dream consisted of the awareness of Medusa's head with the snakes forcing it backwards. In the dream, Medusa's head was in fact his own. He awoke in terror and has never forgotten the nightmare. He had known previously about this fable.

During this hypnoanalytic session the patient had been verbalizing in a manner reflecting a homosexual transference. "I haven't been thinking about anything in particular, just a few images. I don't know; I feel an impatience for something. I was waiting for you to say something and how I'd react to whatever was said. I seem to be relating more to an object, the object being you. At first I had a feeling of wanting to liberate myself, breaking a barrier of some kind. Then there was something fleeting, someone I once knew, her face and how she spoke. Then I became more aware of my physical feelings—arms, hands and legs. I would see your face every once in a while. Once I saw a snake as I saw a few weeks ago in the zoo." There were additional associations pertaining to a need for movement, fantasies of a tunnel, and certain fantasies and recollections of snakes, active and passive. "I looked at it with fascinated repulsion." Later, amid comments related to this, the Medusa's head dream was recalled.

In a note on Medusa's head, Freud offered the decapitation-castration equation (3). He related the Medusa's head theme to various ingredients connected with the castration complex, and stressed the decapitation and snake symbols. In another paper Freud referred to Ferenczi's interest in the Medusa symbolism (2). It is pertinent to mention that Bullfinch describes the Gorgons, of which Medusa was one, as "monstrous females with huge teeth like those of swine, brazen claws, and snaky hair" (1). He pointed out that some writers regarded the

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Gorgons as "personifications of the terrors of the sea." They denoted "The strong billows of the wide open main." This additional Medusa symbolism seems to be consistent, and worth including in the psychoanalytic view of the mythological item.

At the time the present patient told about his Medusa dream, he had as yet been involved neither in heterosexual nor homosexual experience. His speech and manner were effeminate. He preferred the company of women and felt closer to them. Sexual impulses were strongly repressed. He denied much interest in sexual concerns in general.

Writing about Athena wearing "this symbol of horror" on her dress, Freud said, "And rightly so, for thus she becomes a woman who is unapproachable and repels all sexual desires—since she displays the terrifying genitals of the Mother."

Enhanced recall of varying degree has long been associated with hypnotic functioning. The qualitative features of such recall are linked with the nature of the hypnotic transference as is the timing in the emergence of specific memories. The patient's associations as noted above suggest the general matrix for the emergence of the Medusa's head symbolism to which little or no attention or further observations have evidently been made since Freud gave it his attention forty years ago.

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BOOK REVIEWS

LEMKAU, PAUL V. *Basic Issues in Psychiatry.* Charles C Thomas, Springfield, Illinois, 1958. viii + 106 pp. $3.50

To cover the basic issues in psychiatry in something less than 106 printed pages would seem to be impossible. Yet this slim volume well lives up to the promise in its title. Unfortunately, the style of presentation is disappointing.

This book contains five lectures. The first three deal with the magnitude of mental health problems and with possible organic and psychologic preventive measures. The last two chapters cover therapy and administration. All five are straightforward and wholesome, yet at the same time wise and thoughtful. The psychiatrist who is called on to speak before lay groups will find this book a valuable source of ideas.

Unfortunately, the book falls far short of what it should be, and since it is so excellent in subject matter, deficiencies in style are doubly disappointing. It reads like the hastily edited transcript of some excellent talks. Redundancy makes for easy listening but becomes unbearable on the printed page. Dr. Lemkau is obviously a master at his subject matter. With a little more effort these transcribed lectures could have been classic essays.

Enoch Callaway, III

BALDINI, GIOVANNI AND RONCORONI, LUIGI. *Radiologia Clinica delle Endocraniche (Clinical Radiology of Intracranial Calcifications).* Casa Editrice Ambrosiana, Milano, 1959. xiii + 392 pp., illus. L. 5000

This volume is written by two radiologists, one of the two (Baldini) also being a neurologist. The presentation of the material is preceded by a discussion about the biochemical mechanism of production of heterotopic calcifications.

The classification of the intracranial calcifications proposed by the authors and followed in the book is as follows.

A. Asymptomatic calcifications
B. Pathological calcifications in:
   1. Intracranial tumors
   2. Infections or parasitic infestations
   3. Hemorrhage
   4. Vascular
   5. In malformations (hemangiomata, etc.)
   6. Of unknown etiology

The x-ray appearance of each type of calcification is described in detail with a great wealth of illustrations and sketches of excellent quality. In addition, the roentgenographic features are discussed in the light of pathological findings. In the 400 pages devoted to the study of intracranial calcifications, the reader will find different and original criteria of differential diagnosis of particular value.

The chapters dealing with intracranial neoplasms, malformations and calcifications of the cerebral basal ganglia are particularly rich both in text and photographic documentation. The bibliography is particularly rich and covers the world's literature on the subject. It is divided in several parts, a bibliographic index being present at the end of each major group of classifications. In addition, a list of monographs and treatises on the subject is supplied.

The neurologist or radiologist interested in this subject will find this volume extremely useful for consultation both as a textbook and as an atlas of this particular type of pathology.

Carlo A. Cuccia

STOOKEY, BYRON AND RANSOHOFF, JOSEPH. *Trigeminal Neuralgia: Its History and Treatment.* Charles C Thomas, Springfield, Illinois, 1959. xv + 366 pp., illus. $10.75

This monograph consists of a detailed and

meticulous presentation of trigeminal neuralgia both from the literature and from the personal experience of the authors. Although the authors state that "no attempt has been made to review the extensive literature," the bibliography contains 551 references. There is a fascinating and most informative 32-page chapter outlining the historical background of the trigeminal nerve and trigeminal neuralgia. The next two chapters contain a complete and enlightening account of the embryology, comparative anatomy, and physiology, and again the interwoven historical data facilitate the interest of the reader. The chapters concerning non-surgical treatment and alcohol injection were written by Dr. Ransohoff, and those on surgical treatment by Dr. Stookey, one of the most senior and distinguished of this country's neurosurgeons. The operations forming the basis of this study consist of 674 patients who had a total of 728 posterior root sections done by the senior author between the years 1925 and 1955 inclusive. No doubt many neurologists and neurosurgeons, upon reading this volume, will believe that too little emphasis has been placed upon their individual medical and/or surgical procedures of choice and will disagree with the authors on the relative merit of certain therapeutic measures. This monograph is highly recommended to all neurologists and neurosurgeons both because of the wealth of material summarized from the literature and especially because of the benefit that accrues from sharing the extensive experience of the authors and the opinions formulated by them on the basis of that experience.

William H. Mosberg, Jr.

MAY, ROLLO, ANGEL, ERNEST AND ELLENBERGER, HENRI F., EDS. *Existence: A New Dimension in Psychiatry and Psychology*. Basic Books, New York, 1958. x + 445 pp. $7.50

This book is likely to be recorded as one of the first American introductions into a crucial contemporary development in the science of man. The substantive "existence" and the adjective "existential" do not indicate a school or a system, but an overall style of experiencing and thinking which today seems to be increasingly prevalent, after a cultural period characterized by a predominantly positivistic and rationalistic view of reality. The core of this cultural trend could be formulated as the insight that it is impossible to think of subject and object, man and the world as separate from each other. This underlying common awareness is expressed in such terms as "encounter," "participation," "Dasein" or "being-there," "Existence or standing-out," "dialogical existence," or "reciprocity of consciousness." The two first chapters of this volume, written by May, describe how this view has developed in Europe, not only in the culture at large but also in that area of the culture which is labeled psychiatry and psychotherapy. When one knows the original European literature concerning this subject or has tried to make this literature digestible for students, one can feel only admiration for the masterful way in which May presents this new awareness—still in full development—to readers unfamiliar with this stream of thought. The next chapter, by Ellenberger, an excellent scholarly recording of the historical development of the phenomenological point of view in psychiatry, sounds less familiar in its phraseology than May's introduction. Finally, the translations of papers and case histories by several European existential psychotherapists, which make up the bulk of the book, may not easily be understood and appreciated. The fault does not lie with the translators. Comparing, for instance, the German text of the Case of Ellen West, written by the Swiss psychiatrist Ludwig Binswanger, with the English version in this book, this reviewer was struck by the care manifested in the translation of a German that must be complex even for German colleagues. Perfect understanding, however, would presuppose some familiarity with European thinkers

such as Kierkegaard, Dostoievski, Nietzsche, Husserl, Jaspers, Heidegger, Marcel, Buber and others who all in their own way contributed to the creation of the contemporary atmosphere on the continent. Those papers were written originally for colleagues who lived in this atmosphere and for whom most of the terms used would have a definite meaning and would evoke definite associations. The same expressions, when lifted out of their cultural surroundings, seem weird and strange, for they unavoidably evoke different associations in colleagues who have studied within a different cultural frame of reference. The use of literal translations appears to be the main weakness of this otherwise impressive volume. We very badly need initiations into this style of thinking and experiencing which are written in the style May used in creating the first chapters of this book, and which refer whenever suitable to the more congenial American expressions of existential thinking (such as the works of G. Allport, Rogers, Schachtel, some of the work of Murray, Angyall, Maslow, Riesman, Snygg, Combs and others.).

May and Ellenberger, in their respective papers, emphasize the importance of this movement for psychotherapy. This announcement of its usefulness for psychotherapy arouses an expectation which is only partly satisfied in the reading of the translated papers to which the first chapters are an introduction. These case reports are primarily brilliant analyses of the various ways of experiencing which are characteristic of patients. They undoubtedly contain a most worthwhile knowledge which emerged during the therapeutic sessions or in the reflection on these sessions. But those analyses do not teach us about the therapeutic relationship itself. More enlightening remarks regarding the therapeutic relationship are found in May's introduction than in the translated papers themselves.

One has to be aware of the fact that not all representatives of existential psychiatry are to be found in this book, and that some of those who are absent write a more familiar language than those who are represented. Important absentees, among others, are Jaspers, Niedermeyer, von Gagern, Medard Boss and Marguerite Sechehaye.

The suggestion on the cover that this book deals also with existence as a new dimension in *psychology* seems unwarranted in view of the fact that the representatives of existential psychology, except for Erwin W. Straus, are conspicuous by their absence. This is understandable in terms of the clinical interest of the authors and of language barriers. Much existential empirical and experimental research with human and animal subjects has been published in Holland by men and women such as Buytendijk, Linschoten, Beets, Langeveld, Perquin, Dresen and van Lennep. Briefly, what *Existence* really contains is an excellent introduction, primarily in psychiatry and psychotherapy, as it developed in the new cultural period, followed by conscientious translations of a few representatives of existential psychiatry who present phenomenological analyses of the experiences of their patients to a public of colleagues who were supposed to have some familiarity with the philosophical and cultural influences prevalent on the European continent today.

This book is a fragmentary introduction in a new, all-pervading cultural stream of living and thinking which it represents only in part. The reader who would define the existential period of culture and its inherent psychology and psychiatry on the sole basis of the translations in this book, will undervaluate the historical evolution which is still in full process. But if he studies this book as a first introduction, he will be in better touch with his time and prepared for the increasing stream of other books and papers which surely will confront him in coming years.

Adrian L. van Kaam

TERMAN, LEWIS M. AND ODEN, MELITA H. *The Gifted Group at Mid-Life.* Stan-

ford University Press, Stanford, California, 1959. xiii + 187 pp. $4.50

The characteristics of gifted persons are always of interest. Here we have an exceptionally valuable description of individuals in their mid-forties, more than 35 years after the initial longitudinal study of them as children was begun. How well this sample of gifted children "paid off" in the sense of living up to their childhood potential, is the main question to be kept in mind in reading this book.

Perhaps more than many of his contemporaries Lewis Terman must have been conscious of the fact that childhood was the pathway to adulthood, not an end in itself. At the time he began this study of a group of 1528 children (age 11) with a mean I.Q. of about 150, he must have had it in mind that he would follow them into adult life. Earlier publication of the data on childhood had considerable impact in that they forcefully refuted some stereotypes about the nature of children of high level intellect. Although some unevenness in abilities was noted in the gifted children, "the deviation of gifted children from the generality is in the upward direction for nearly all traits; there is no law of compensation whereby the intellectual superiority of the gifted is offset by inferiorities along non-intellectual lines." On the average these adults—as gifted children—tended to be higher than unselected children in a variety of intellectual, emotional, moral, physical, and social traits rated by parents and teachers.

In a real sense the age of 45 is still too young to know how these intellectually very superior individuals will turn out in detail, but 45 is a sufficient age to reveal the main tendencies of the group. This group is still rising in achievement and its high water mark has yet to be reached. In many respects these people are maintaining their above average position in the population. In this 36-year follow-up, "No negative correlations were found between intelligence and size, strength, physical well-being, or emotional well-being." It seems to be a generally good thing to be intellectually gifted, both as a child and as an adult. More than ten times the number of individuals in this group graduated from college than in the general population. About 14 per cent of the men and four per cent of the women earned doctorate degrees; many of these are having illustrious and expanding careers. In addition to fulfillment of promise in the eyes of the world, the authors rightfully point to the many intangible aspects of achievement. Less dramatic than being listed in *Who's Who* is the achievement of the man or woman who devotes his talents in life to doing well with daily problems, in realizing personal goals and establishing a good family life. It is harder to measure this kind of behavior in comparison with occupational achievement, yet even here the gifted are reported to do somewhat better than average.

A longitudinal study extending over 35 years is an impressive testament to both the foresight and vigor of the original investigator. At the same time the investigator is inviolably married to methods and subjects selected long ago. Methods and topics change and a present reader might wish for more or different kinds of data than those presented. Perhaps today we would be less enchanted with the I.Q. as a dominant feature of the project, yet who could have predicted the psychological research interests of 1959 from the vantage point of 1921? Perhaps the value of this work is reflected in the continuing wish—as one reads—for "more," more data, more information, more analyses. This in itself is a tribute Terman would have appreciated.

The results of this study are more relevant to generalizations about what will happen to groups, rather than leading toward tight predictions about individuals. As one reads the book one is impressed by the fact that it is a good thing generally to be intellectually gifted, to test high on intelligence tests. Associated with being intellectually

gifted are many diffuse advantages or correlates as a child and as an adult. Seen individually, however, the promise and rewards are not so great as to make for regret in those who as children do not show themselves as intellectually gifted. Similarly, the results show little promise of a simple method of selecting the gifted at an early age for special investment and intellectual diet. There are so many individuals who follow presently unknown courses of development toward their adult achievement that an open mind is certainly needed in making individual predictions. This is not a contradiction of this study, but an implicit part of it.

James E. Birren

KARPMAN, BENJAMIN, ED. *Symposia on Child and Juvenile Delinquency.* Psychodynamic Monograph Series, Washington, D.C., 1959. 364 pp. + index, illus. $10.00

This book is a transcribed recording of five symposia conceived and chaired by Dr. Karpman, and held at meetings of the American Orthopsychiatric Association. They have already been published separately in the Journal of Orthopsychiatry, with some parts omitted. In this book, both the original papers and the discussions are presented in full "for the benefit of the public at large." This reviewer is still at a loss to determine just how the public at large will benefit from this compilation of impressions, debates, struggles with semantics, gropings and sometimes downright confusion.

The topics of the symposia are, respectively: The Psychopathic Delinquent Child, Psychopathic Behavior, A Differential Study of Psychopathic Behavior in Infants and Children, Psychodynamics of Child Delinquency, and Basic Emotional Factors in Delinquency. The participants are physicians (with three exceptions) who have achieved some prominence in the clinical study and treatment of acting out disturbed children.

As one might expect from the titles, there is a great deal of overlap and consequently repetitiousness. Certain themes which keep recurring are: the contributions to delinquency of heredity, disease, social dislocation, and parental behavior; the meaning of psychopathic personality—and of delinquency; the role of deprivation; the problem of diagnostic subgroupings; pathological mechanisms; issues in therapy (are psychopaths treatable?); and so on. The method for dealing with these matters is primarily that of dynamic clinical psychiatry, with reliance on case history material obtained through interviews, observation, and psychotherapy. Some of the histories are interesting and provocative, but the data for resolving the conceptual issues which these histories represent are either lacking or ignored by most of the contributors.

Although a number of interesting points and points-of-view are raised by some participants, the most important contribution of such a book is to demonstrate glaringly the need for good controlled research in this field and the wisdom of appreciating and integrating into one's thinking the varied research that has already been done.

David Rosenthal

GIBBS, FREDERICK A., ED. *Molecules and Mental Health.* Published for the Brain Research Foundation by J. B. Lippincott, Philadelphia, 1959. xii + 189 pp., illus. $4.75

This slim volume with its intriguing title presents the proceedings of two privately-supported conferences sponsored by the Scientific Council of the Brain Research Foundation. The title of the book reflects more or less accurately the content of the first conference, "Amines in relation to brain function and behavior," since this conference deals with the issue of whether or not twisted metabolism of amines, especially epinephrine, norepinephrine and acetylcholine, underlies the twisted thinking of the schizophrenic (to paraphrase Gerard). However, the title bears little relation to the

content of the second conference, "ACTH treatment of hypsarhythmia," which discusses primarily the successful treatment of a specific variety of infantile convulsions by means of adrenal steroids.

In both conferences, panels of experts discuss in informal fashion some of their latest findings. The emphasis, particularly in the first meeting, is clearly on discussion of details among experts rather than on the systematic, orderly communication of information to the reader. The comments after each paper are reported in full; the active, sometimes heated interchange between speakers and discussants conveys well the fluid state of knowledge in this field and the highly controversial nature of the current candidates (ceruloplasmin, taraxein, tryptophan, acetylcholine) for the role of the twisted amine in schizophrenia.

Since there is no summary or overview of the papers in the conference on amines (and this is a serious omission) it may be well to provide one by means of a brief account of the biochemical approaches to mental illness.

The chemist searches in more or less empirical fashion for some naturally-occurring substance, X, usually in the blood or urine, which schizophrenic patients possess exclusively or possess in larger amounts than do normal persons (or the reverse). Abood's paper describes one such substance, ceruloplasmin, alleged to have this property. Alternatively, the chemist may begin with a substance that produces psychotic-like behavior (an hallucinogen) in human subjects. The biological action of the agent which elicits the "model psychosis" is studied, again in the hope of discovering that the concentration of some naturally-occurring substance, X, is modified by the hallucinogen (the papers by Hoffer on ergot hallucinogens and by Abood *et al.* on a new class of psychotogenic substances illustrate this approach). Once having found X, the specific process or processes by which X is metabolized is investigated, in order that its biological origin and fate may be understood. When these facts are known, the chemist may attempt by direct or indirect biochemical means to restore this substance to "normal" levels, in hopes of producing a beneficial effect on psychotic behavior. Such experiments are described in the papers by Pfeiffer *et al.* on acetylcholine and by Zeller on tryptophan metabolism. The opposite kind of experiment may also be performed, *i.e.*, one attempts to elicit psychotic behavior in human subjects by producing directly or indirectly "abnormal" titers of X. The paper by Heath *et al.* on taraxein presents such experiments.

In almost every paper included in this conference one is struck by the disparity between the great amount of knowledge about the biochemical mechanisms and the relative lack of knowledge about the behavior. To be sure, the chemists may disagree as to whether it is vitamins B and C or tryptophan and ceruloplasmin which differentiate the schizophrenic from the normal person, or whether adrenochrome is present in the brain or not. However, their techniques are sufficiently advanced so that, for example, by radioisotopic labeling of a specific atom on the molecule of some metabolic substance, they may trace its pathway and final disposition with considerable precision. By contrast, the behavioral analysis is in most instances crude. The test of the psychic potency of an agent is still largely whether or not it produces "psychotic-like" behavior; agreement as to what this means is far from unanimous. Moreover, although the chemical methodology is usually routine and often well-standardized, the precision in the design of the behavioral aspect of the study appears often to be a matter of personal taste and the level of sophistication frequently poor. Thus, Heath remarks in connection with the issue of whether or not controls are necessary in testing the effect of taraxein, "We think that the whole experiment ought to be thrown out if one has to worry about whether someone did or did

not receive it (*i.e.*, taraxein). If it (the behavioral effect) is not more marked, it is what we consider an insignificant experiment and we throw it out." In contrast with this are the impressive efforts (although still in the early stages of development) of Elmadjian and the group at Worcester to identify different types of emotional states and to relate them to differential excretion of epinephrine and norepinephrine.

It is to be hoped that further developments in this area will involve increased attention not only to the structure of the molecules but to the details of the behavioral analysis, as well, for this may prove to be the limiting factor in psychochemical research.

The second conference, "ACTH treatment of hypsarythmia," is shorter than the first, generated less controversy among the participants and is consequently simpler to review. In 1957 Sorel reported that ACTH was effective in the treatment of a specific form of infantile epilepsy. This disease, which is characterized by paroxysmal jerking of the whole body, and which is invariably accompanied by progressive mental deterioration, was labeled 'hypsarythmia' by the Gibbses on the basis of the unique electroencephalographic features of the disorder. The conference, of which this account is a kind of *Festschrift* to Sorel, was called to bring together individuals who had either tried Sorel's technique (this includes papers by Sorel, Stamps *et al.* and Low), who knew something about brain disorders relevant to hypsarythmia (papers by Kellaway, Poser, Lichtenstein and Garvin) or who knew something about ACTH (general discussion by Dorfman, Pfeiffer and others). In this way, two purposes could be achieved: experiences with the therapy could be shared; some rational account of the success of the therapy could be provided. The first purpose was certainly achieved; there seems to be general agreement that the treatment is successful in halting or reversing the course of the disease, including the mental retardation, in the majority of cases, if it is started early. The second purpose was not achieved; those working with hypsarythmia understand why administration of ACTH cures this disease about as well as those working with schizophrenia understand why administration of appropriate amines do not. There is, however, a distinct advantage in possessing a treatment that one knows will work, and several possibly fruitful hypotheses to account for the effect of ACTH were advanced.

In sum, the best feature of the book is the technical discussion by the participants of the two areas towards which the conferences were directed. The most serious weakness is the lack of a summary or overview and appraisal of the papers within each conference and some rational explanation for having included two quite dissimilar bodies of information within the same publication.

Allan F. Mirsky

BRAZIER, MARY A. B., ED. *The Central Nervous System and Behavior* (Transactions of the First Conference). Josiah Macy, Jr. Foundation, New York, 1959. 450 pp., illus. $5.25

This volume presents the transactions of the first of a series of multidisciplinary conferences on The Central Nervous System and Behavior sponsored by the Josiah Macy, Jr. Foundation with the cooperation of the National Science Foundation. The Macy Conferences are designed to promote communication between scientists and to stimulate creativity. In addition, in this particular series of conferences, it was proposed to review both historical and also recent studies conducted in Russia in order to familiarize Western scientists with the development and present status of work and thinking in Russian laboratories. To this end approximately half of the present volume is devoted to a survey of Russian contributions to the study of the central nervous system and behavior. The presentation of this material is well conceived and

beautifully executed. A series of 107 illustrations provides a pictorial survey of the historical development of neurological and behavioral studies, from the authorization of an Academy of Science by Peter the Great in 1724 to Pavlov (1849–1936) and Bechterev (1857–1927). The early members of the Academy were scientists imported from the West, including such men as the mathematician, von Euler. Lomonosov, "the father of Russian science," the first Russian-born professor to be appointed to the Academy, later was the founder of the first Russian University. In the nineteenth century he was followed by a number of famous men—Lobachevsky, Lebedev, Popov, Mendeleev, Metchnikov and others. Neurophysiology started with Sechenov—who first described central inhibition. His training in Germany, Austria and France emphasized a mechanistic and deterministic view of the functions of the brain and introduced a holistic approach to neurophysiology—influences which since have remained dominant in Russian laboratories. Vasily Danilevsky, Tarkhanov, Wedensky and Ukhtomsky are referred to briefly, but the careers, work, accomplishments and theories of Pavlov and Bechterev are illustrated in considerable detail. Throughout the survey attention is called to the interests of Russian scientists in the arts and humanities and in the social movements of the nineteenth century. The survey thus provides a bird's-eye view of Russian neurophysiology and of the academic and cultural setting in which it developed.

Following the pictorial survey, the careers and contributions of the Russian neurophysiologists are discussed in more detail. Members of the conference, approaching the material from different points of view, have provided a many-faceted picture, some of the recent parts including personal experiences. Particular attention is paid to analysis of the physiological theories developed and their change as new experiments were done in other laboratories. For example, the relations of Bechterev's concepts of the "associative reflex," with Pavlov's "conditional reflex," and the different connotations of our current term "conditioned reflex" are considered in some detail, together with the hypotheses concerning the brain mechanisms involved. A number of common theoretical terms used in the Russian literature such as "functional lability," "parabiotic phase," "inhibition," "irradiation," "spread," "extinction," and so on are discussed and defined in terms of the experiments which gave rise to them. This discussion is an important contribution as it is critical and well-documented and will prevent much confusion in the future. For example, the Russian expression "parabiotic phase" refers to phasic changes in excitability of tissues such as nerves, etc. and has no relation to the use of "parabiosis" in our literature.

The phenomena dealt with in Russian experiments are also discussed to a certain extent in the light of more recent work. Of particular interest is the consideration of extinction. Dr. Roger W. Sperry summarizes a good deal of data indicating that well-established conditioned responses may be behaviorally "extinguished," but are not lost. In other words, durable effects can be demonstrated. Dr. Sperry also emphasizes the fact that no past or current theories provide an adequate model for the mechanism of learning or conditioning.

The second half of the volume presents brief reviews of current American work directed at determining intracranial and intracerebral events temporally or functionally related with the types of behavior studied in conditioning experiments. The material is divided roughly into experiments using stimulation of the brain—either as a "signal," as a "reinforcement" or as a "punishment"—and into experiments recording electrical events in the brain during the course of the various stages of conditioning and extinguishing different patterns of behavior. The review of these data is compre-